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Elio Raviola, obituary

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Elio Raviola, a scientist and professor emeritus in the Department of Neurobiology at Harvard Medical School passed away on December 23, 2023, at the age of 91. Elio was born on June 15, 1932, in Asti, Italy, son of Giuseppe and Luigina (Carbone) Raviola. While at Ghislieri College in Pavia in 1953, as a third-year medical student, Raviola met Giuseppina d'Elia (1935-1986), a first-year student at Collegio Castiglioni-Brugnatelli, just across the street from Ghislieri. Both worked on similar research topics, and Giuseppina became a member of the same Institute of Anatomy at the University. Elio and Giuseppina were married in Pavia in 1960. With his medical degree Raviola spent several years engaged in training as a specialist in neurology and psychiatry, managing a unit at the local mental hospital. Elio obtained his Ph.D. in 1963 at the age of 31 and was an Assistant Professor in the Institute of Human Anatomy from 1958 to 1971.

PAVIA TO BOSTON, 1965-70

In 1960, Elio found himself frustrated by the pace of his academic progress and felt that he needed mentorship. He took a train to meet with Professor Rodolfo Amprino (1912-2007) at the University of Bari. Amprino was a student of the famous Italian anatomist Giuseppe Levi (1872-1965). The schools of Golgi and Levi had been intellectually in disagreement with one another at the time, as Levi was an acolyte of the Spanish neuroscientist Santiago Ramón y Cajal (1852-1934). So, when Elio asked Amprino if he would take him in his department, Amprino suggested that such a change would destroy Raviola's career in Italy. Amprino suggested that Elio go to the U.S. for several years for a new experience, and then later transfer to his lab in Bari. In 1963 Amprino provided Elio with the address and the name of an Italian scientist working in the US, Rita-Levi Montalcini (1909-2012). From Levi-Montalcini he received advice for a possible research activity in the United States. Then Elio hoped to spend time in the labs of Don Fawcett at Harvard University. Fawcett invited both Elio and his wife Giuseppina to work for a year as Research and Teaching Fellow, respectively, in Anatomy at Harvard Medical School, from 1965-66. On arrival to Boston, Elio and Giuseppina, were given an empty lab space by Fawcett, who told them to make a list of reagents and other equipment they needed to demonstrate their scientific aptitude in short order. The trial period went well. However, while he was offered a position by Fawcett, Elio and Giuseppina returned to Italy due to her developing an illness, requiring treatment. She recovered in Italy, and they were pursued by Fawcett to return to Boston. In 1970 Raviola accepted Fawcett's invitation as Associate Professor of Anatomy.

Elio remembered the day, October 23, 1970, arriving at Logan Airport and being greeted by various professors in the department, including Susumu Ito (1919-2015), Jean-Paul Revel (1932-2021), Betty Hay (1927-2007) and others. The couple led the introductory medical school courses in Anatomy at Harvard and Boston University, respectively, while also developing successful, separate, research careers focused on the retina.

Over many years he developed a very close friendship in the department, with Torsten Weisel. It was a very collaborative scientific environment, in which everyone was proud of the success of mentors and colleagues like Weisel, Fawcett, Stephen Kuffler (1913-1980), Ito, David Hubel (1926-2013), Baruj Benacerraf (1920-2011), and others from the very beginning. Elio would say, "Don was an extraordinary man. Torsten is an extraordinary man. Sus was an incredible scientist".

SCIENTIST AT HARVARD MEDICAL SCHOOL, 1970-2023

Elio became Associate Professor of Anatomy in 1970, Professor of Anatomy in 1974, Bullard Professor of Neuroanatomy and Professor of Ophthalmology in 1989, Bullard Professor of Neurobiology in 1993, and Professor Emeritus in 2013. He dedicated himself to research on the nervous system for sixty-six years. He led a laboratory in the Departments of Anatomy and Neurobiology at Harvard Medical School for fifty-three years, from 1970 to 2023. Elio received numerous offers for leadership roles in other departments early in his Harvard career. These included offers for chairs at Cal Tech, the position of Dean at Washington University in Saint Louis and the University of Pennsylvania, and an invitation from Johns Hopkins as well. He stayed at Harvard because, simply, he didn't want to be a Chair, and was happy in the department at Harvard.

Elio evolved to become an expert of cell biological, electrophysiological, and molecular techniques, solving problems of structure, connectivity and physiology of the retina, the part of the eye that received and processes signals from light. He was interested in how the retina can encode information from the visual scene, and then send the encoded information to the brain. Over six decades he contributed to evolving, foundational knowledge in the field of neurobiology, while continuously learning new methods to effectively respond to new scientific questions.

With Wiesel, 1981 Nobel laureate in physiology or medicine, he developed not only a wonderful friendship, but also an experimental model of myopia (near-sightedness). They studied how alterations of the visual experience during the postnatal growth of the eye leads to myopia. They discovered that the eye elongation that leads to myopia is mediated by the nervous system, specifically by growth regulating chemicals produced in the retina itself. Also, with Ramon Dacheux II (Ray) in the 1980's he conducted novel studies of the way in which the photoreceptors, the cells that receive and process light, interact with secondary neurons in the initial processing of visual information.

After Raviola obtained an NIH grant entitled "Cell Communication in the Retina", Ray built a setup for visual stimulation and intracellular recordings from the rabbit eyecup and thus began a fruitful collaboration that lasted 14 years.

Throughout the years of their collaboration, twice a week Ray and Raviola were recording from rabbit retinal cells and injecting them afterwards with horseradish peroxidase (HRP). The experiments lasted from ear-

ly in the morning through most of the following night and Ray would then sleep at Raviola's house. They spent more time together than both did with their families and became intimate friends. Ray was a virtuoso of the job well done and was endowed with unusual manual skills: his were the hands of an artist. Very few things in life are as rewarding as sharing the joys and frustrations of scientific discovery with a trusted colleague of great intellectual integrity and the same aspiration for excellence. Ray and Raviola devoted their investigations to the neural network encoding the signals of rod photoreceptors in the rabbit retina: they analyzed the structure of rods isolated from the adult retina and correlated the response properties of horizontal cells with their morphology and synaptic connections with the photoreceptors (1982, 1990). They obtained the first electrophysiological recordings from H1 horizontal cells in the rhesus macaque and showed that these cells were homologous to the axon-bearing horizontal cells of other mammalian retinas (1990). At the time, there were uncertainties on the response properties of rod bipolars, until Dacheux and Raviola showed that they responded to light with a transient-sustained depolarization dominated by rods and had a center-surround organization of their receptive field. Therefore, the dyad synapse established by rod bipolars with the two depolarizing amacrine cells postsynaptic to them (A2 and A17 or S1/S2) was excitatory and sign-conserving (1986, 1987, and 1989).

This work was followed by a series of papers with Enrica Strettoi (now a senior investigator in the Institute of Neurophysiology of the National Research Council in Pisa, Italy), in which the synaptic connections of the neurons that carry rod signals to ganglion cells, rod bipolars, A2 amacrine and cone bipolars, were reconstructed from continuous series of thin sections analyzed with the electron microscope. These papers established unequivocally that 'the rod pathway in the rabbit piggybacks the cone pathway and thus gains access to a single set of ganglion cells that are driven by both rods and cones (1990, 1992, 1994).' (Visual Neuroscience, 2007;24:445-447). Elio had several other collaborations within the department and with experts at other institutions. Most often these collaborations were grounded both in professional respect, and in loving friendship forged over both warm exchanges of scientific ideas, as well as time spent together outside of the laboratory. This included Tom Reese, Steve Sugrue, and others. Through the 1990's Elio was able to transition from an anatomist to cell biologist, to a molecular biologist. He had most recently directed his efforts to characterizing the role of each neuron cell type, focusing on the ways in which amacrine cells in the retina uniquely release

the neurotransmitters dopamine and GABA, as well as seeking to understand the specific function of this mechanism in human adaptation to light. Using a multidisciplinary approach with colleagues he identified all the transcripts present in dopamine amacrine cells, discovered the presence of the common clock-related proteins in those cells (with Stefano Gustinich et al.), showed that some amacrine cells spontaneously release dopamine and GABA through different mechanisms (with Michelino Puopolo et al., and Hajime Hirasawa et al.), and he described a unique set of synaptic contacts made by dopamine amacrine cells at nodal points of the retinal network needed to optimally shape retinal light adaptation (with Massimo Contini et al., Richard Masland et al.). He described much of this work as follows: "Our understanding of the computations carried out by neural networks in the central nervous system is limited by our incomplete knowledge of the diversity of cell types and the multiplicity of their functions. In the retina, over fifty cell types encode the spatial, temporal, and chromatic parameters of the incoming light stimuli to generate the messages of action potentials that travel to the brain along the fibers of the optic nerve. We have combined molecular techniques with microscopy and electrophysiology to study a rare cell type in the retina, the dopaminergic amacrine (interplexiform cells)." (Raviola E. A molecular approach to retinal neural networks. Functional neurology. 17(3). 2002.). Constance L. Cepko, Bullard Professor of Genetics and Neuroscience at Harvard Medical School remembers when Elio approached her at the turn of the 1990's about her supporting his learning newer methods in her laboratory. While he was a visiting professor in her lab, he behaved as a visiting post-doctoral student: "He came to my lab to learn molecular biology. He kept the most beautiful, neat, and complete lab notebook that I had ever seen. I used it as an example to my students and he was so courageous, at his august stage in life (in his 60's), to become a novice in a new field. He was able to learn enough to return to his lab and use the new methods to make a transgenic mouse that labelled the dopaminergic neurons that he wanted to understand. It led to a beautiful study of the synapses of that cell type, made possible by his mastery of anatomy and physiology, combined with molecular biology." Moving into the new millennium and beyond, Elio continued to be deeply engaged in the intellectual life of the Department of Neurobiology at HMS and found the department to be "extraordinary." Of the strengths of the department, he recently wrote: "A varied approach to neuroscience, total freedom to express oneself, a friendly atmosphere of openness, mutual respect and generosity that leads to rapid circula-

tion of ideas and collaborations, and a Chair concerned about the welfare of the faculty.” He saw the mission of the department to be one of “advancing knowledge of the brain by combining rigorous molecular, cellular and behavioural techniques.” He greatly appreciated both formally and informally convening with his departmental colleagues in an environment that encouraged the sharing of ideas on a wide range of topics related to science, culture and the personal. During COVID-19, he continued going into the department five days per week for most of the pandemic, when physical return to the medical school was permitted. He continued to have close rapport with several close friends and colleagues in the department. He felt at home in the Department as well as an incredible feeling of gratitude for the community of scientists and friends he had there.

Raviola did not only deal with the retina and the nervous system. It is important to mention that the clearest morphological evidence concerning the existence of the blood–thymus barrier may be attributed to the collaborative work published in 1972 by Morris Karnovsky and Elio Raviola. Raviola and Karnovsky, using HRP as a permeability tracer, demonstrated that the venules at the corticomedullary junction are the site of leakage for blood antigens, while the capillaries draining the cortex are largely impermeable. Other permeability studies have confirmed the existence of a blood–thymus barrier, which allow the access to low molecular weight tracers, while most exclude high molecular weight particles.

TEACHING OF ANATOMY, 1970-2002

He was responsible for the Introduction to Anatomy course for entering, first-year Harvard medical students. He directed the course for thirty years, from 1972 through 2002, also lecturing extensively in Histology and Neurobiology to both medical and graduate students. His excellence as a teacher was recognized instantly by students and faculty alike. In 1972 Raviola received the Boylston Society Award for excellence in teaching at Harvard Medical School, as well as multiple subsequent pre-clinical teaching awards. He was called by some students “The Italian Master” In the dissection room he not only taught the students methods of dissection and anatomical detail, but also reviewed the history of anatomical discovery over the past several thousands of years.

With a remarkable memory, he could quote Cicero, Julius Caesar and Dante verbatim from his high school lessons.

Elio was known for his remarkable lectures, which were a dramatic and artistic performance, cherished by

students for decades. He would come to the lecture hall early in the morning and draw detailed, beautiful pictures in colour on the black board, using French art chalks.

Between 1986 and 2002 Elio co-led the human anatomy course at Harvard Medical School with Daniel Goodenough. His excellence as a teacher was documented in the television documentary series *Chronicle and Nova*. Trudy Van Houten, former Director of the Clinical Anatomy Course and Co-director of the Human Body Course at Harvard Medical School, notes that “His lectures were legendary: beautifully organized, original and ingenuous, wonderfully humorous, and full of surprises. They were carefully crafted lessons that included exactly the information students needed, combined with the brilliance and charm necessary to keep students captivated from the first to the last sentence and in memory even decades later. They were, first and foremost, lessons directed at the students who listened to them. His lectures remain unforgettable...I also remember his incredible tact when I was a new anatomy instructor in his anatomy lab at HMS and how generously, and diplomatically, he shared both his knowledge of anatomy and his knowledge of effective anatomical teaching. I also recall, with admiration, how he managed the extraordinary feat of dividing his time, relatively evenly, among eight dissection tables all clamouring insistently for his attention.” “Elio was an amazing scientist and extraordinary person. His aesthetic sensibilities influenced his beautiful anatomical studies, as well as his students and admirers,” says Carla Shatz, Professor of Neurobiology at Stanford University and a pioneer in early brain development “Elio was a scholar and intellectual of the old school. He had a sense of his discipline’s history and tried to convey the same in his lectures, demonstration, and tutorials. His colleagues appreciated these attributes as well,” notes James Adelstein, Executive Dean for Academic Programs at Harvard Medical School from 1978-97.

MENTORSHIP OF YOUNG SCIENTISTS, AND SERVICE TO HARVARD AND SCIENCE IN ITALY

Elio was a dedicated mentor to many young scientists as well as a trusted advisor to leaders at Harvard Medical School.

Michelino Puopolo, Associate Professor at Stony Brook University notes that “when I first arrived in Boston in 1998, Elio was like a second father to me.”

Richard Born, Professor of Neurobiology and a former director of the HMS Ph.D. Program in Neuroscience recalls: “Elio was such a wonderful man, colleague and scientist”.

Matthew Lawrence at the St. Kitts Biomedical Research Foundation notes that “He was a source of wise and valued counsel at every important professional step from pursuing graduate training, then medical school and ophthalmology, and subsequent commitments to translational science and institution building”.

Elio was very active in efforts to strengthen Italian science, including the creation of the Italian Institute of Technology and the establishment of the Giovanni Armenise-Harvard Foundation. In advising the Armenise-Harvard Foundation, which supports basic scientific research at Harvard Medical School and in Italy, he worked in a focused way to help the careers of young, promising Italian scientists. He mentored Italian post-doctoral fellows in his laboratory, including Massimo Contini (University of Florence), Stefano Gustincich (Italian Institute of Technology Genova), Adalberto Merighi (University of Turin), Michelino Puopolo (Stony Brook University), and Enrica Strettoi (Institute of Neuroscience at the Italian National Research Council in Pisa). He cherished engaging with Italian collaborators with independent careers, including Giovanni Berlucchi (University of Verona), Emilio Bizzi (Massachusetts Institute of Technology), Saverio Cinti (University of Ancona), Cesare Montecucco (University of Padua), Enrico Mugnaini (Northwestern University), and Paolo Pinelli (University of Pavia, Catholic University in Rome, University of Milan).

Enrica Strettoi, Director of Research at the Institute of Neuroscience at the Italian National Research Council in Pisa notes that: “Elio was my undisputed scientific mentor, the one who believed in me when I was little more than a little girl, who convinced me that I could do it and win a place in the research academy. His enthusiasm, passion for microscopy, intuition of the importance of what you see but which not everyone is able to decipher, they infected me many years ago. I hope I have passed on a bit of all this also to my students, to whom I often turn using his own words...He was so generous, both in a human capacity and scientifically, and was for me my first home in professional terms, the place where I would mentally go when I feel in difficulty or had fear that I was not up to something scientifically that seemed too complex. I was incredibly fortunate to cross paths with him and equally lucky to maintain his respect and esteem. I went to him in very difficult moments as well as in those moments of great professional recognition: his consistency has always been admirable and striking, as he knew how to be himself on every occasion, with wit, clarity, and passion.”

He received honorary degrees from the University of Ancona in 1996 and the University of Turin in 2002.

In 2002 he was also awarded the Ottorino Rossi Award from the University of Pavia, presented to a scientist who has made an important contribution to research in the field of neurosciences.

Stefano Gustincich, Principal Investigator at the Italian Institute of Technology in Genoa, recalls 30 years of memories when “Elio was a father-like figure nurturing my growth as both a scientist and a human being.”

Massimo Contini, Professor at the Università Degli Studi di Firenze notes that “I loved him. It was certainly one of the fundamental meetings of my life. I can’t summarize the meaning of this friendship in a letter, we were lucky to have had him in our lives. The memory of his intelligence, his irony and his energy will remain forever.” Saverio Cinti, Professor at the University of Ancona, notes that “I always had the ambition to consider myself his student and his younger brother. I will always remember him with great affection, and I will greatly miss his passionate stories of the Pavia period. His words have always been an example and my entire academic life has been influenced by him, especially the great passion for scientific research so expertly pursued and appreciated about him throughout the world.” The period of his university education as a student at the Ghislieri College, in a University of Pavia that was still epically “Golgian”, because it was populated by professors who had known Camillo Golgi, has always remained alive in his mind. And throughout his life he always showed a great passion for the history of medicine. With one of us he wrote a historical-critical article on Golgi’s discoveries and theories of brain functioning (Raviola and Mazzarello, 2011).

Cesare Montecucco, Emeritus Professor at the University of Padua notes that “Elio put truly exceptional care and energy into advancing his students... He was a great man. We were different ages, but we came from the same world, and we immediately understood each other’s way of seeing life and science.”

Elio served the Departments of Anatomy and later Neurobiology at Harvard under the leadership of five Chairs: Don Fawcett, Betty Hay, Carla Shatz, Michael Greenberg, and David Ginty. He worked in the Departments of Anatomy and Neurobiology from October 1970 to April 2023. Raviola saw his mentorship of students (both medical and research) and colleagues in the department as central to his usefulness as he advanced in age. Into his 80s, he served on the HMS Subcommittee of Professors, the Prizes and Awards Subcommittee, the Honors Committee, the Armenise-Harvard Foundation Junior Faculty Grant Review Committee, the Armenise-Harvard Foundation Scientific Advisory Board, the Armenise-Harvard Foundation Italian Schol-

arship Advisory Committee on Career Development Awards, the Excellence in Mentoring Award Selection Committee, the Council of Mentors Subcommittee, and he chaired meetings of the Graduate Student Advisory Committees.

With a great pride in being a part of the American scientific experience, Raviola noted the difficulty of feeling neither Italian nor American, “a person without a country.” Fundamentally identifying himself as a scientist, Raviola had a clear vision for the evolution of science in the U.S. and globally; he connected the evolving scientific landscape to the political environment. He was concerned that “the best young scientists are no longer coming” to the U.S., a research environment which he felt had offered him the freedom and support to manifest his own creative capacities and gifts to the ultimate degree.

REFERENCE

Elio Secondo Raviola (June 15, 1932-December 23, 2023). Remembrances from his Family, Friends and Colleagues on the occasion of his Memorial Service April 21, 2024. The American Academy of Arts and Sciences Cambridge, Massachusetts, USA.



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The anatomical wax collection at the University of Bologna: bridging the gap between tradition and scientific innovation

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Abstract. The “Luigi Cattaneo” Anatomical Wax Collection belongs to the network of Museums and Collections of the University of Bologna. It is closely related to the Anatomy Centre of the Department of Biomedical and Neuromotor Sciences of the University of Bologna, and holds a significant place in the history of medicine, art, and scientific innovation. This review explores the museum’s rich historical background, its cultural importance, and its role in promoting the encounter between the past and the present. Preserving the legacy of anatomical wax modelling, the museum adapts to modern education and to research needs. It bridges artistic expression and scientific knowledge, emphasizing the importance of art as a tool of medical education. In this context, augmented reality, 3D models, CT scan and new methods of communication, integrate tradition and progress, expanding anatomical exploration. As part of the University of Bologna, the Collection catalyzes interdisciplinary collaboration, unlocking new scientific avenues. It works as a bridge through time, uniting craftsmanship, exploration, and knowledge-seeking in the study of the human body.

Keywords: wax collection, Anatomy Centre, tradition, innovation, education, human body.

INTRODUCTION

Museums of anatomy and pathology hold significance in preserving anatomical specimens and their high-quality reproductions, as well as their role in education and research (Mariño Gutierrez et al., 2019). Although museums experienced a moment of great prosperity in the eighteenth century, they were characterized by a progressive decline and a dramatic loss in the following historical period. Nevertheless, there is currently an increasing interest in revitalizing and acknowledging the importance of these collections, especially thanks to the development of anatomical teaching in medical education and its relevance in the advancement of medical research. The “Luigi Cattaneo” Anatomical Wax Collection, belonging to the network of

Museums and Collections of the University of Bologna, fits perfectly in this cultural context. It is based in the historical institute of Human Anatomy of the University of Bologna, today known as Centre of Clinical Surgical Experimental and Molecular Anatomy (Anatomy Centre). It is formed through the merger of two pre-existing collections and showcases the artistic and scientific legacy of wax modelling in the study of human anatomy and pathology. Its anatomical collection includes wax models, natural bones, dry and platinated preparations, mummified and formalin-preserved specimens. These models illustrate the various conservation techniques of the human body, from the antique mummification process to the contemporary plastination technique.

Anatomical wax modelling has an ancient origin but rose to prominence in fourteenth century in Italy with the cult of votive artefacts. With the advent of Neoclassicism, this art continued to survive in scientific fields (Ballestriero, 2010). The primary goal of wax modelling art was to effectively communicate the discoveries that had made anatomy the most advanced of the biological sciences (Riva et al., 2010). Indeed, the need to show the true nature of the human body and its pathologies in the most realistic way possible, prompted medical science academics to enlist the help of different artists, in order to create three-dimensional drawings and models. This signaled both an educational-scientific and aesthetic value and gave rise to an intense and fruitful collaboration between anatomists and artists, sanctioning the meeting between science and art.

Therefore, this review focuses on the collection's historical background and highlights its cultural significance, while emphasizing the incorporation of scientific innovation in providing an immersive educational experience. Consequently, the museum represents a testament to the enduring connection between art and science.

1. HISTORICAL BACKGROUND

Interest in anatomical wax models spread throughout Europe during the eighteenth century (Pastor et al., 2016), first in Bologna with Ercole Lelli (1702-1776), a talented artist with a great interest in anatomy, Giovanni Manzolini (1700-1755) and Anna Morandi (1714-1774), spouses anatomists and experts in wax modelling, and then in Florence with Felice Fontana (1730-1805) and Clemente Susini (1757-1814) (Ballestriero, 2010). Indeed, wax is a malleable material that has been used for different purposes since ancient times by Egyptians, Greeks and Romans and throughout the centuries many anatomical artists used wax modelling due to the remark-

able mimetic likeness obtained, far surpassing any other substance (Rodriguez and Parish, 2020). This material is particularly flexible, easy to color, and it can be decorated using organic tools such as body hair, hair, teeth and nails. With the beginning of Neoclassicism these characteristics made the realistic nature of wax models seem repulsive, and the practice of artistic ceroplastics started a slow decline. Moreover, religious authorities began to discourage the worship of saints and votive offerings and many of the most talented votive artists moved toward anatomical ceroplasty (i.e. Susini). However, despite the disappearance of the use of wax modelling techniques from an artistic point of view, there was a notable growth in its use for educational and scientific purposes for the study of normal and pathological anatomy, obstetrics, veterinary medicine, zoology and botany (Ballestriero, 2010). During the Renaissance, the new scientific interest in anatomy motivated artists and physicians to study post-mortem bodies. In this context, wax again proved to be the most suitable material to meet the needs of artists considering the extreme difficulty in finding usable corpses and the understandable unwillingness to dissect and examine unpreserved dead bodies. Indeed, only later it was found the way to preserve the cadaver for investigative and teaching purposes. Therefore, for a long time, wax was considered a necessary alternative method capable of providing an accurate reproduction of the various organs of the human body.

2. CULTURAL IMPORTANCE

The Luigi Cattaneo Anatomical Wax Model Collection, inaugurated in 2002, represents the result of the merger of two separate display sections previously existing in the Institutes of Human Anatomy and Pathological Anatomy (Figure 1). It shows a rich collection of anatomical preparations and wax models dating back to the nineteenth century, most of them concerning pathological anatomy. With the nineteenth century, in fact, the demonstrative spaces of ceroplasty expanded to new fields of medical knowledge. From normal anatomy they moved on to pathological anatomy and the depiction of clinical manifestations of multiple morbid pictures. The creation of pathological models was thus the logical consequent development of the success of models devoted to normal anatomy. Once again, life-like appearance of the anatomical waxes, resembling human flesh, were able to blur the lines between a real body and a representation illustrating pathological malformation. According to the "*modus operandi*" of the Bolognese School, these specimens were arranged in the Anatomical Cabinet in



Figure 1. Anatomical Wax Collection “Luigi Cattaneo”. Detail of the sign above the entrance commemorating Ercole Lelli, the founder of the Bolognese Ceroplastical School.

order to realistically reproduce the pathological cases observed during autopsies and dissections. They usually represented supporting material to research articles that were read and discussed in front of the scientific community. Indeed, these materials on clinical cases became a powerful tool in the pursuit of educational and scientific aims. From this point of view, the Collection is an example of how ceroplastics took on particular value in the nineteenth century for the dissemination of scientific and artistic culture.

The achievement of having made known the use of wax modelling as a teaching aid for human anatomy is generally attributed to the Sicilian abbot Gaetano Giulio Zumbo (1656–1701) better known as Zumbo (Riva et al., 2010; San Juan, 2018). He was succeeded by the previously mentioned Ercole Lelli, founder of the Bolognese Ceroplastical School, who was commissioned to create an anatomical collection of models made of durable material (Maraldi et al., 2000). This artist considered the knowledge of human anatomy essential to characterize the language of the human body. Among his activities, he produced a wax model of two kidneys joined at the lower end (“horseshow” kidneys), which had been discovered during a “public dissection” (Riva et al., 2010). Tables showing colored wax models of normal kidneys and horseshow ones, are preserved in Palazzo Poggi Museum in Bologna and definitively won over the academicians of the Institute of Science. He also realized the so-called *notomie*, statues of skinned bodies, in clay,

wood and wax (Cushing, 1937). Their anatomical perfection, obtained through a careful representation of post-mortem bodies used for dissection, served as a reference model for the study of anatomy. In this way, the foundations for the art of wax modelling of anatomical preparations for medical practice studies at the University of Bologna, were laid (Maraldi et al., 2000). Subsequently, other artists’ wax models, dating back to the eighteenth century, and mainly the Anna Morandi’s works, the first Italian female anatomist and ceroplastical artist, were well-recognized all over Europe and are now exposed and Palazzo Poggi Museum (Rosito et al., 2004).

Among the works belonging to the collection and hosted in the Anatomy Centre of the Department of Biomedical and Neuromotor Sciences of the University of Bologna, of notable interest is the collection of over two thousand skulls (Figure 2) belonging to the Bolognese anatomist Luigi Calori (1807-1896) (Galassi et al., 2016). This collection testifies the important development in the anthropological studies for the human racial classification in the first half of the nineteenth century.

Moreover, the museum’s collection includes pigmented beeswax models of normal and pathological anatomy created by other important ceroplastical artists of the late eighteenth and nineteenth centuries, belonging to the Florentine or Bolognese wax sculpture school: Clemente Susini, Giuseppe Astorri (1785-1852) and Cesare Bettini (1801-1885). Wax modelling was basically a craft technique and each school adopted modifications and variations of the original method. The Florentine School, represented by Clemente Susini, differentiates itself for the use of wax reinforced by iron and wood supports and for the creation of plaster molds for mass production. Instead, the Bolognese School shaped the wax models using real bones (Manzoli et al., 2022). In this context, wax models became valuable tools for medical education, providing a tangible representation of the human body’s intricate structures. During the Enlightenment period, anatomical wax models gained recognition not only for their educational value but also for their artistic merit. Artists meticulously crafted lifelike representations of human anatomy, joining science and art. This fusion of disciplines helped elevate anatomical wax modelling to a form of scientific artistry.

It is also appropriate to underline the importance that wax models had in medical education and public outreach through the representation of both authentic and simulated smallpox pustules in humans and cows, of which the Luigi Cattaneo Collection preserves two models (Figure 3) (Zampieri et al., 2011). These ones were aimed at educating not only doctors but also a wider audience of health professionals. This historical



Figure 2. Collection of skulls. Professor Luigi Calori's collection of skulls hosted at the Anatomy Centre of the Department of Biomedical and Neuromotor Sciences of the University of Bologna.



Figure 3. Wax model of smallpox pustules created with didactic and diagnostic purposes. The model is part of the “Luigi Cattaneo” Anatomical Wax Collection closely related to the Anatomy Centre of the Department of Biomedical and Neuromotor Sciences of the University of Bologna.

context underscores the enduring importance of wax models as effective tools for medical education and the broader communication of critical health information.

A perfect example of the “*modus operandi*” followed by anatomists and pathologists of the Bolognese School in the nineteenth century, is represented by the clinical case described by Cesare Taruffi (1821–1902), the first

professor of Pathological Anatomy at the Bologna School of Medicine (Quaranta et al., 2020). In a scientific paper he reported the case of a man with pronounced prognathism and skeletal deformities, an unrecognized case of acromegaly. As anticipated, to fully describe clinical cases to the scientific community, anatomists and professors typically used to prepare dried anatomical specimens and create tables, engravings, and wax replicas. All Taruffi's examined samples currently reside at the ‘Luigi Cattaneo’ Anatomical Wax Collection in Bologna (Quaranta et al., 2020). Because of his observations of craniofacial and skeletal deformities, Prof. Taruffi's article is often cited as a scientific contribution to the origin of the definition of acromegaly in the era preceding Pierre Marie (the one who for first introduced the term acromegaly) (Mammis et al., 2010; Pearce, 2006). This fact underlines the cultural importance that wax samples could have in the anatomical-scientific field. All in all, the models present in the Anatomical Wax Collection in Bologna, reflect the evolution of anatomical understanding, capturing the scientific and artistic perspectives of their time. Preserving this anatomical, technical, and educational heritage allows for an appreciation of the contributions made by early anatomists and artists to the field of medicine. Indeed, independent of the material used, whether wood, wax or clay, which varied according to the periods and the different workers, anatomical models were always considered merely craft works confined to hospitals or faculties of medicine

and have survived to this day because of their scientific interest (Manzoli et al., 2022).

3. SCIENTIFIC INNOVATION AND LEAP INTO THE MODERN ERA, PRESERVING TRADITIONS

The encounter between past, present and future is fundamental to the educational mission of the Anatomy Centre of the Department of Biomedical and Neuromotor Sciences of the University of Bologna, to which the Anatomical Wax Collection is closely related. Just as cultural vicissitudes and new trends in medical education had changed the role of dissection as a method of teaching anatomy in medical schools in the past, giving way to wax models and plastination, scientific progress has inevitably changed also the role of these last techniques (Papa and Vaccarezza, 2013; Ghosh, 2015). In the museum context, while the wax models continue to retain their historical charm, the need for the integration of modern technologies is increasingly evident, not only to improve the visitor experience, but also to complement the classes of dissection of modern medical and surgical students. Interactive laboratories, virtual reconstructions, and multimedia presentations provide a bridge between the past and the present, allowing for a comprehensive exploration of human anatomy and pathologies, involving not only medical students or people belonging to the scientific community, but also kids of all ages and their families. Indeed, the Anatomy Centre continuously adapts to incorporate innovative teaching methodologies. Traditional wax models are nowadays supplemented with tools based on the combination of augmented reality (AR) technologies and tangible 3D printed models that can be studied and manipulated by students/trainees, thus favoring a three-dimensional and topographical learning approach (Cercenelli et al., 2022). These advancements offer students and researchers new ways to study and comprehend the complexities of the human body (Ma et al., 2016). Indeed, several recent studies have reported the positive effects of using AR in medical training, with increased learner immersion, a higher engagement and a better perception of the studying time (Cercenelli et al., 2022).

Consequently, incorporating AR into medical education alongside traditional methods might prove advantageous for students' academic and future professional activities (Neri et al., 2024). Therefore, the presence of the collection inside the Anatomy Centre fosters collaborations between anatomists, clinicians, and researchers, continuously bringing to light new forms of communication in the medical and scientific fields.

The Centre recently obtained funding from the European Union for the purchase of a Computed Tomography (CT) tool. The challenge is to apply modern morphological and structural investigation techniques to the materials collected in the museum, opening up new perspectives in the enhancement of this historical and scientific heritage, in terms of both better knowledge and dissemination and recovery of the educational role of the waxes (Figure 4). Imaging techniques in medicine have evolved with great rapidity and innovative solutions and, in this context, CT is planned to be applied to the examination of the museum's anatomical waxes. The incorporation of a CT scanner within the museum's conservation toolkit stands as a significant advancement in the preservation and dissemination of historical artefacts. This sophisticated equipment plays a pivotal role in the digitalization of museum items, thereby aiding in their conservation. By converting physical objects into high-resolution digital forms, the CT scanner ensures that these cultural treasures are preserved for posterity, while simultaneously reducing the need for physical handling, which can often lead to deterioration. Furthermore, this technological adaptation extends the reach of the museum's collection, allowing a broader audience to access and appreciate these artefacts in their digital form, democratizing access to cultural heritage. Additionally, the CT scanner's ability to perform extensive material analysis unveils intricate details of the artefacts, offering insights into their composition, construction, and historical context. Such detailed examination enriches the understanding of these items, enhancing both scholarly

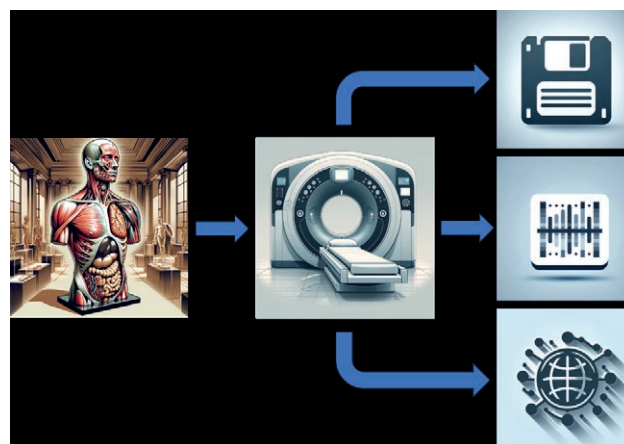


Figure 4. Use of Computed Tomography (CT) tool. Reconstructing anatomical models through CT scans results in a virtual representation, providing insights into the various techniques used and contributing to the development of a multi-level accessible virtual museum project.

research and the general public's engagement with the museum's collection. Altogether, the CT scanner emerges as an invaluable asset, revolutionizing the way museums conserve, share, and study historical artefacts (Peccenini et al., 2015; Tian et al., 2022, Maher, 2020).

Nevertheless, in an era where modern technologies offer increasingly precise alternatives to traditional bodies' dissection, preserving the age-old practice of examining post-mortem bodies remains crucial. Since 2013, a whole body donation program was set up at the Institute of Human Anatomy of the University of Bologna (De Caro et al., 2021) and in February 2020 the law n. 10/2020 entitled "Rules on the disposal of one's body and post-mortem tissues for the purposes of study, training, and scientific research" was approved, and the Institute was appointed National Reference Centre for body donation by the Ministry of Health (Orsini et al., 2021b). The dissection rooms located within the Centre (Figure 5), playing the role of modern "surgical theatres", ensure ongoing clinical education and training through the use of both traditional gross anatomy and innovative technology (Orsini et al., 2021a, Marre and Villet, 2020), achieving once again a harmonious balance, perfectly blending modern elements with tradition. This endur-

ing tradition ensures that surgeons and doctors receive a comprehensive understanding of anatomy that cannot be replaced by advanced technologies alone, underscoring the durable importance of hands-on learning in the field of medicine. Practicing with post-mortem bodies, not only imparts a deep understanding of anatomy but also cultivates essential qualities of respect, compassion, and empathy for patients, a dimension that modern technologies can only partially replicate, further emphasizing the enduring value of this tradition.

In this context, also the "graphic medicine" (GM) workshops that the Anatomy Centre promotes fit perfectly (De Stefano et al., 2023). These workshops, focused both on human anatomy and on body donation, contribute to raising awareness among students and members of the scientific and non-scientific community on complex and delicate topics, which, unfortunately, are not talked about enough. Therefore, the anatomical wax museum and graphic medicine converge in promoting the understanding of human anatomy and the awareness about body donation. While the museum preserves the tradition of anatomy and expands its understanding through the use of modern technologies, GM offers a new communicative approach to engage medical stu-



Figure 5. "Giovanni Mazzotti" Dissection Room. Dissection room is located at the Anatomy Centre of the Department of Biomedical and Neuromotor Sciences of the University of Bologna.

dents in studying and understanding sensitive topics such as body donation, before using it with the general population.

4. CONCLUSION

The Anatomical Wax Museum in Bologna stands as a remarkable convergence of history, science, and art. This museum encapsulates the enduring value of anatomical and pathological preservation while adapting to the demands of modern education and research. The wax models, meticulously crafted through a centuries-old tradition, bridge the gap between scientific knowledge and artistic expression. Rooted in the historical legacy of anatomical wax modelling, the museum preserves the tangible evidence of a collaborative journey between anatomists and artists. It records the transition from artistic representation to a scientific tool that revolutionized medical education and research. This transformation reflects not only the shift in societal perspectives but also the innate human drive to comprehend the complexities of our own bodies.

Furthermore, the museum's embrace of technological innovation, and increasingly creative methods, signifies a harmonious blend of tradition and progress. Augmented reality, tangible 3D models and graphic medicine, propel anatomical education into the digital age and into a more engaging and ethical context, empowering medical students to engage with anatomy in unprecedented ways. This fusion of past and present expands the boundaries of anatomical exploration and enriches the understanding of human health and disease. Overall, it is clear that both post-mortem bodies dissection, anatomical wax models and modern interactive systems based on artificial intelligence represent strong innovations in medical teaching for their respective historical period. In this context, the Anatomy Centre is able to offer all these opportunities, creating a strong impact and representing a reference point in the academic world.

As an integral part of the Department of Biomedical and Neuromotor Sciences at the University of Bologna, the museum represents a hub for interdisciplinary collaboration, uniting anatomists, clinicians, and researchers in a collective pursuit of knowledge. The anatomical wax models, once tools for study, have now evolved into conduits for unlocking new realms of scientific discovery.

All in all, the Anatomical Wax Museum in Bologna serves as a bridge across time, offering a profound glimpse into the evolution of anatomical understanding. Waxes new value is no longer related to the functionality they had in the past but it is related to their ability to tell a story,

to be witnesses of a reality that represents the past but can still carry us to the future. Waxes and the museum's collection itself, are at the same time concrete and symbolic manifestation of the scientific progress. They also represent the point from which research started and from which it can measure where it has arrived. They remind us that the exploration of the human body is a timeless endeavor, harmonizing artistic craftsmanship, scientific exploration, and the unquenchable thirst for knowledge.

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DATA AVAILABILITY STATEMENT

All information can be found at the following link: <https://site.unibo.it/centro-anatomico/it>

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Rare case of adult truncus arteriosus from the Vernon-Roberts Museum of The University of Adelaide (Australia)

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Abstract. Persistent truncus arteriosus (TA) is a congenital heart disorder that is characterized by various anomalies that can be fatal without corrective medical intervention. Surgical techniques were initially developed to correct this condition in infants, consequently, this has led to a paucity of scientific research on adults with TA. In this case study, the authors examine TA in the heart of an adult. The specimen derives from the pathology museum from the Vernon-Roberts Museum of The University of Adelaide. Given the rarity of individuals surviving with TA into adulthood, more scientific attention needs to be invested in unique people with TA in order to provide a comprehensive understanding of this condition as well as adequate medical treatment and care.

Keywords: truncus arteriosus, congenital disorder, Australia, clinical cardiology, pathology museum.

ANATOMICAL AND CLINICAL INTRODUCTION

Truncus arteriosus (TA), also known as persistent truncus arteriosus is a rare congenital heart abnormality. Truncus arteriosus is a single arterial trunk exiting the heart (by way of one semilunar valve) to supply systemic, pulmonary, and coronary arteries (Abbott 1936, Anderson et al. 1957, Sharma et al. 1985, Abid et al. 2015, Martin et al. 2016). Other anomalies are occasionally associated with TA such as pulmonary arterial hypoplasia, interrupted aortic arch (IAA), ventricular septal defect (VSD) and quadricuspid aortic valves (Martin et al. 2016, Alamri et al. 2020). Although, preva-

lence of TA varies between studies, it can safely be noted that it accounts for <4% of congenital heart disorders (Hoffman 2011, Martin et al. 2016, Nabati 2017, Safi 2018, Alamri et al. 2020).

TA is typically detected during the neonatal period or early childhood, where symptoms of pulmonary hyper-circulation induced congestive heart failure and cyanosis are evident (Martin de Miguel et al. 2022). It has been estimated that 34% of patients with TA have DiGeorge Syndrome (22q11 deletion) (Lupski et al. 1991, Laohaprasitiporn et al. 2008). Furthermore, diabetic mothers have a 12 to 13-fold risk of having an infant developing TA compared to their non-diabetic equivalents (Ferencz et al. 1997).

In 1798, Wilson produced the first account of TA (Wilson 1798, Mavroudis et al. 2015). Later Buchanan (1864) presented an examination of undivided TA in a six-month-old infant, while Shapiro (1930), and Lev and Saphir (1942) made important contributions to defining and classifying TA. Although the surgical technique of pulmonary artery banding (PAB) was conceived by Muller and Dammann in 1952, pulmonary artery banding was only introduced in the 1960s with substandard outcomes in infants (Muller and Dammann 1952, Craig and Sirak 1963, Williams et al. 1963, Goldblatt et al. 1965, Mavroudis et al. 2015). However, it was not until 1968, when correction of truncus arteriosus abnormality was achieved by using a homograft of the ascending aorta, that also included a heart valve. This technique established a new outflow from the right ventricle to the pulmonary trunk (Dwight et al. 1968).

MATERIALS AND METHODS

In this case study, the authors examine TA in the heart of an adult individual. The specimen (Fig. 1) derives from the Vernon-Roberts Museum, The University of Adelaide. Given the rarity of individuals surviving with TA into early and middle adulthood, it is useful to describe this case from a morphological perspective to provide a comprehensive understanding of this condition and adequate medical treatment and care.

CASE DESCRIPTION

According to the information supplied by the Vernon-Roberts Museum, The University of Adelaide, the heart specimen is derived from a 45-year-old female. Patient anonymity was maintained. No mention was provided of the decedent's ethnicity, any other morbidi-

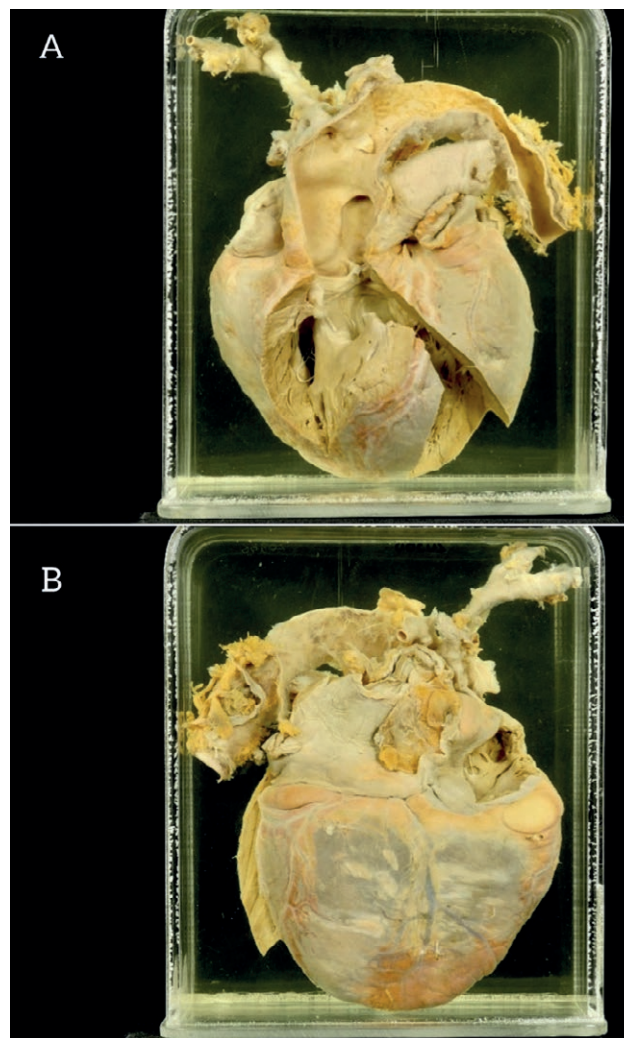


Figure 1. Frontal (a) and posterior (b) view of the heart with evidence of the persistent truncus arteriosus.

ties or other personal details. At the age of 35 years the decedent had been diagnosed with truncus arteriosus. The decedent had died from a cardiac arrest on the 6th day after admission to a hospital. Her clinical diagnosis had revealed tachycardia, polycythaemia (erythrocytosis), atrial fibrillation and right/left ventricular failure. The right ventricular wall was hypertrophic. There was a 25 cm atrioventricular septal defect, as well as an overriding single great vessel and a posteriorly arising pulmonary artery. At death the decedent's heart was grossly enlarged and weighed 680 grams.

Although TA prevalence is very low, its signature hemodynamic pathology requires immediate medical intervention. Without corrective surgical treatment, mortality occurs in \approx 80-90% of neonates in the first year of life (Ebert et al. 1984, Thompson et al. 2001, Kharwar

et al. 2014, Nabati 2017, Alamri et al. 2020). However, even after successful surgical intervention, there is an increased need for long-term cardiac management due to possible continuing complications (Chen et al. 2016, Puri et al. 2017, Bhansali and Phoon 2023). High mortality associated with TA is often due to it causing hypertensive pulmonary arterial pressure with subsequent onset of pulmonary disease (Sharma et al. 1985). Even with such a high mortality rate, there is a small percentage of individuals who can live with TA up until early middle age (i.e. 45-50 or 60-65 years). Unfortunately, there has been comparatively little scientific research on adults with TA. One reason for this could be persistent medical focus on pediatric cases. Second, there have been few individuals who have been able to live with TA beyond early middle age (Porter and Vacek 2008). Therefore, it is unfeasible to systematically monitor and examine this sparse group. Additionally, since it is unclear how individuals managed to survive with TA into adulthood, both outward reach and treatments are difficult.

CONCLUSION

This case shows the importance of anatomical and pathological collections both for educational and research purposes in the fields of biomedicine and anthropology, as previously stressed both in the context of anatomopathological museum studies and the assessment of cardiovascular diseases in the past (Nesi et al. 2007, Henriques de Gouveia et al. 2021). Future research on such specimens could be aimed at combining morphological and clinical data with radiological and genetic investigations capable of offering a comprehensive phenotypic and genotypic background on a pathology still of great relevance for clinical medicine.

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Congenital Horner Syndrome in art: the case of a historical Austro-Hungarian soldier

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Abstract. One of the most important characteristics, which determine facial appearance, is eye colour. Among the different conditions that causes an alteration in the normal iris pigmentation is congenital Horner Syndrome. Here we describe a case of right unilateral segmental heterochromia iridum in the historical portrait "Portrait of an unknown soldier" displayed at the Ferdinandeum Tyrolean State Museum (Innsbruck, Austria). Along with heterochromia, the sitter also displays right anisocoria, miosis, and mild ptosis of the upper and lower lids. This case highlights the interest of artists for modification of facial appearance in order to represent the sitter in the most possible realistic way.

Keywords: heterochromia iridum, anisocoria, miosis, ptosis, Renaissance, Austria.

Segmental heterochromia is rare in humans. The majority of cases of heterochromia iridum is benign and is not associated with underlying disorders. However, this condition needs monitoring, since it may be associated with different diseases, such as congenital Horner Syndrome, Parry-Romberg Syndrome, Waardenburg Syndrome and Fuchs heterochromic iridocyclitis (Rehman, 2008).

Here we present a case of right unilateral segmental heterochromia iridum in the "Portrait of an unknown soldier" (Inventory number Gem 697) displayed at the Ferdinandeum Tyrolean State Museum (Innsbruck, Austria) (Figure 1). The painting has been prepared in the style of the school of Rubens. However technical investigations suggest that the portrait presents a

possibly 19th century repaint of an older canvas. Therefore, an exact dating of the painting is currently not possible. Along with heterochromia, the sitter also displays right anisocoria, miosis, and mild ptosis of the upper and lower lids. This triad of clinical features is consistent with congenital Horner syndrome. Facial anhidrosis, another feature which may be present in Horner Syndrome (HS), cannot be appreciated in a canvas.

First described in animals by Claude Bernard (1854), the syndrome was identified in humans in 1863 by Weir-Mitchell and colleagues. However, it was not until 1869 that the Swiss ophthalmologist Johann Friedrich Horner (1831-1886) attributed it to oculo-sympathetic paresis (Kanagalingam, 2015; Jeffery et al., 1998). The palsy manifests when lesions of one of the three neurons forming the oculosympathetic pathway (the central neuron, the preganglionic neuron, or postganglionic neuron) occur the pupil and the eyelids is interrupted (Kanagalingam & Miller, 2015; Jeffery et al. 1998).

Depending on the affected neuron, a first order HS, second order HS, or third order HS, is diagnosed (Kanagalingam & Miller, 2015; Jeffery et al., 1998). In general, the first and third order neurons are more often involved in adults whereas, in paediatric patients, the second order neuron is the most likely. The lighter coloured iris is always on the side of the HS since sympathetic stimulation is needed for the deposition of the pigment in the stroma of the iris (Pollard et al., 2010). Denervation impairs melanin pigmentation making the affected eye lighter (Ropper & Brown, 2005).

Heterochromia iridum typically is a feature of congenital HS, but it can also occur in lesions with onset before 2 years old (Jeffery et al., 1998; Pollard et al., 2010). The most frequent cause of paediatric acquired HS at the second order neuron is neuroblastoma of the paravertebral sympathetic chain (Pollard et al., 2010). Given the mature age of the sitter, the diagnosis of neuroblastoma can be excluded. Also Parry-Romberg Syndrome, Waardenburg Syndrome and Fuchs heterochromic iridocyclitis (Rehman, 2008) can be excluded, since their clinical features would have not been consistent with military life. Similarly, except from birth trauma or post-viral infections, lesions due to other serious and life-threatening acquired conditions can be reasonably ruled out (Pollard et al., 2010).

All clinical features displayed in adult-onset acquired HS (i.e. Pancoast tumour, dissecting carotid aneurysm, middle cranial fossa neoplasm, brachial plexus trauma, brainstem stroke, carotid artery ischaemia and migraine) can be confidently excluded, since heterochromia iridum is not manifested in these conditions (Kanagalingam & Miller, 2015; Jeffery et al., 1998;



Figure 1. Portrait of an unknown soldier, oil on oak wood, 72,5 x 55,4 cm. On the rear side an Anvers burn mark. Inventory number Gem 697. Legat [bequest] Josef Tschager 1856 (provenience: Collection Ritter von Prohaska, auction Mollo (Vienna) 12. March 1820). While the profession of the sitter was inferred from the military uniform, no further personal information is available. The canvas is attributed to the school of Rubens and has been tentatively dated between 1577-1640. The canvas is currently held by the Ferdinandeum, the third oldest national Museum of the Austro-Hungarian Empire, which was founded in 1823 and named after Archduke Ferdinand II.

Pollard et al., 2010). Furthermore, in adults with HS, acquired heterochromia is extremely rare. So far, the disorder has never been reported in patients with an acute or recently acquired HS (Diesenhouse et al., 1992).and only a few cases of long-standing, acquired Horner Syndrome with heterochromia iridis are mentioned in biomedical literature (Diesenhouse et al., 1992).

Taking in account that the unknown sitter was a soldier, the presence of an artificial right eye should be considered. However, although the use of eye prosthetics dates back to Antiquity (up to 4800 years ago) (Pine et al., 2015; Moghadasi, 2014); the ability in manufacturing eye prosthetics reached high technological levels in the late 16th century with Venetian glass blowers, along with lens makers, able to produce realistic but fragile glass eyes (Pine et al., 2015). High quality glass eyes were also

produced in Augsburg where a manufacturing centre was active until the Thirty Years War (1618-1648) (Pine et al., 2015). However, based on the pictorial representation, eye trauma is very unlikely, since no scarring in the eyelids can be appreciated. This absence of evidence leads us to exclude the presence of a glass eye.

This pictorial representation of congenital HS adds to another we previously identified in a portrait displayed in Vienna's *Kunsthistorisches Museum* (Austria) (Bianucci et al., 2020). In that canvas, which originally belonged to the pictorial collection of Archduke Ferdinand II of Tyrol (1529–1595), a sitter, another unknown adult nobleman, appears to be affected by paediatric HS in the right eye. These cases highlight the peculiar interest of both the artists and their patrons to depict physical modification from the normally perceived anatomy of the eyes and ocular eyelids. In addition, these examples strongly indicate that (at that time) individual traits, including pathological changes, were documented accurately raising the value of the paintings as realistic depictions.

The main limitation that needs to be emphasised is the lack of contemporaneous documentary sources and remains of this individual to triangulate the findings. However, the portrait nonetheless offers a visual image that gives insight into the past presentation of a relevant medical condition.

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Exploring the genetic and pathobiological pathways of talipes equinovarus: a short narrative review

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Abstract. Talipes equinovarus (TEV), also known as club foot, is one of the common congenital foot deformities. TEV deformity includes the components of osteochondral tissues namely supination, or inversion of the subtalar joint (hind foot varus), forefoot adduction deformity (metatarsus adductus), exaggerated midfoot arch (cavus) and limited ankle dorsiflexion (equinus). Its prevalence ranges from 0.5 to 2.0/1000 live births. It is hypothesized that TEV manifestation is due to molecular genetic defects that are influenced by environmental factors. The deformity had been recognized for centuries, but its main cause remains elusive. This narrative review summarizes the literature data that have accumulated over the past few decades on the environmental, molecular, and genetic factors along with the pathobiological mechanisms underlying TEV and analyze the role of these factors in the development of this disease. TEV segregates in families with both autosomal dominant and recessive mode of inheritance or autosomal dominant with incomplete penetrance. This supports the involvement of the genetic component underlying TEV. Genetic factor underlying TEV is further supported by the fact that a much higher concordance rate is seen in monozygotic (32%) rather than dizygotic (2.9%) twins. Various genetic studies including candidate gene association studies, copy number variation analysis, linkage analysis, whole exome sequencing and whole genome sequencing have shown the involvement of certain genes in the development of TEV. The research work done so far is still deficient for the exact genetic cause in families with TEV as most studies have focused on the sporadic cases and the genetic causes documented so far are still speculative. TEV is considered as a multifactorial congenital deformity where both genetic and environmental factors disrupt the normal mitotic division of the cytoskeleton in the lower limbs and ultimately leads to the formation of deformed foot. Hence, large multiscale, multicenter collaborative studies using genetic techniques like genome wide association studies (GWAS) with single nucleotide polymorphisms scan and linkage analysis in large families are required.

Keywords: talipes equinovarus, genetic, pathology.

INTRODUCTION

Skeletal disorders include a series of different conditions where the development and architecture of the chondro-osseous tissue is adversely affected leading to deformities of the musculoskeletal system. TEV is one of the most common congenital abnormalities affecting the limbs characterized by deformity of the foot with four components of osteochondral tissues, hind foot varus, forefoot (metatarsus) adducts, exaggerated midfoot arch (cavus) and equinus (1,2). The deformity is illustrated in Figure 1.

The birth prevalence of TEV varies from 0.5 to 2.0/1000 live births (3). In the low to middle income countries, it varies between 0.15 to 2.03/1000 live births (4). TEV incidence is high in the Māori population in New Zealand which is explained by the genetic load carried by closed societies (5). Around 80 % of all the reported cases of TEV are classified as isolated club foot also called non syndromic, while the other 20% are associated with other clinical abnormalities, thus called syndromic. Syndromic TEV is more commonly associated with myelomeningocele and distal arthrogryposis, multiple epiphyseal dysplasia, Larsen syndrome (LS), Lambert syndrome, and Ehlers-Danlos syndrome (EDS) (6,8) as shown in the Figure 2. The studies performed on the isolated TEV are carried out during their childhood, however no data is available for these cases in their adulthood to elaborate if they have delayed presentations of other features. Male to female ratio is 2:1 which is not variable in different societies (7). Kursi et al in 2008 explained the polygenic and multifactorial pattern of inheritance where females would also be more likely to transmit clubfoot to their children thus having



Figure 1. An infant with bilateral club foot (Courtesy of orthopedic unit, District headquarter hospital Rawalpindi Pakistan).

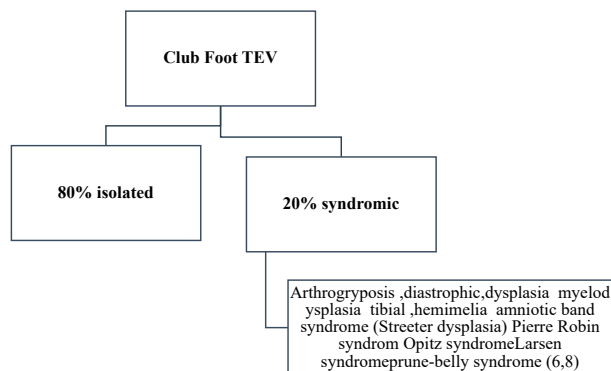


Figure 2. Showing the presentation of TEV.

the Carter affect. Club foot can be unilateral (30-40%) or bilateral (60-70%). TEV manifests a large variety of bio-molecular genetic defects which are further influenced by environmental factors (9).

Historically, TEV was also described by Hippocrates during his era (10). Egyptian Pharaoh Tutankhamen in 1332 was also featured to be suffering from club foot (11). A 17th century painting of a dubbed *clubfoot child* by Jusepe de Ribera still hangs in the Musee du Lavre (12). Since old times, a lot of work and advancements have been achieved in the management of TEV. But the main cause of this deformity remains evasive. In this review, our focus will be on the molecular genetic factors and pathobiological mechanisms underlying TEV.

ETIOLOGY

Despite multiple theories, the exact cause underlying this deformity is still unknown. It is multifactorial where both environmental and genetic factors are thought to play a significant role (13). Some of the environmental factors like maternal psychological distress during pregnancy, alcohol use, parental age, parental education, and birth season have been excluded due to lack of significant statistical association (14). Hippocrates postulated that, during the intrauterine life of a fetus, increased intrauterine pressure compressing the lower limbs plays a role in the development of this deformity. But later, studies showed that congested fetus with oligohydramnios, twins' pregnancy, large babies and primigravida fetuses are not affected by club foot. (15). Moreover, it has also been proved that TEV can be diagnosed even at the second trimester of pregnancy before the intrauterine pressure rises. (16) The most common and congruous environmental factor involved in etiology of this anomaly is exposure of the women

to the tobacco smoke during pregnancy (17). Previous studies showed that tobacco smoke is biotransformed in modulation with N-acetylation genes *NAT1*, *NAT2*. It is supported by the studies that variations in *NAT1*, *NAT2* genes are associated with TEV (18). Moreover, decreased acetylation activity of *NATE 2* gene polymorphism is also found to be associated with TEV (18,19). Additionally, genetic variation in smoking metabolism genes were also studied in relation to clubfoot where it is found that perturbation of *CYP1A1 gene results in* adverse effects on the development of lower limb. (20).

As TEV is segregating in families with both autosomal dominant and recessive mode of inheritance, concordance rate is more in monozygotic (32%) than in dizygotic twins (2.9%) (21,22,23). Various genetic technologies have been used to identify the genetic defects involved in the development of TEV. Candidate association studies, copy number variation analysis, linkage analysis, whole genome sequencing and whole exome sequencing have pointed out the involvement of certain genes in the development of TEV (13). But the genetic molecular regulatory network underlying the TEV is yet to be identified. Other studies showed that the TEV is a multifactorial deformity of the lower limb where genetic factors are predominant but modifiable by environmental factors (24,25).

GROSS PHENOTYPIC ABNORMALITIES OF THE TEV

In TEV the tibia and fibula bones are slightly shortened due to the incomplete developmental process. (26,27). Hence, distal tibial metaphyseal fractures due to diastasis in the tibiofibular joint have been reported in several cases while doing forced dorsiflexion and eversion of the ankle joint. (28,29,30). Relations of talus bone with other abnormal bones divided into different subgroups like medical subluxation of the navicular bone on the talar head and medially subluxated cuboid bone over calcaneal head, which ultimately leads to restriction of movements in the ankle joint. (28,29). However, some bone anomalies in TEV like small dome shaped deformation is associated with better range of movements in the ankle joint (31).

Congenital hypoplasia of the calf muscles even after the treatment of TEV was reported (32). The total number of the muscle fibers was normal, but they showed type 1 fiber atrophy, deficiency of type 2b and increased number of types 2c muscle fibers suggested abnormal development of these muscle fibers in TEV cases (33).

GENETICS OF TEV

Usually, mutations in genes coding for the contractile proteins of skeletal myofibrils like *MYBPH*, *TPM2*, *TNNT3*, *TPM1*, *MYH13* and *MYH3* are involved in the TEV (34,35). However, Gurnett et al. in his study of 31 patients out of whom 20 were suffering from familial clubfoot TEV patients could not detect mutations in *TNNT3*, *MYH3*, and *TPM2* genes (35). Although he found several previously undescribed single-nucleotide polymorphisms of unknown importance.

GENES IMPLICATED IN TEV

PITX- gene

PITX1 gene participates in the development of the hind limb primarily the legs and feet. The first brachial arch, an embryonic structure located at the base of the brain, is also found to preferentially express *PITX1* (36,37). A study of six proband of Ghanaian parents were reported with co-occurrences of orofacial clefts (congenital malformations of the face and palate) and club foot with variable genetic causes (38). The defect in bronchial arches explain the co-occurrence. Most studies show that genetic defects in *PITX1* can cause lower limb developmental deformities such as developmental hip dysplasia, patella hypoplasia, tibial hemimelia, preaxial polydactyly together with bilateral TEV (39,40,41,42). Moreover, copy number variations as well as haploinsufficiency of *PITX1* have been shown to play a crucial role in the development of isolated clubfoot. (44,45).

TBX4- gene

T-box family, T-box factor 4 (*TBX4*) is a known transcriptional factor and its expression has been observed in multiple organs and tissues (46). Knock out studies revealed that *TBX4* gene has a significant role in the development of the lower limbs and the respiratory pathways (47). Hence, mutations in the *TBX4* lead to skeletal dysplasia and pulmonary hypertension due to developmental lung diseases (48). Specifically, mutations in *TBX4* gene have been reported with pulmonary developmental disorders and lower limb deformity (49). Moreover, microduplication of the 17q23.1q23.2 region which involves *TBX4* has been identified in familial cases of TEV (50).

HOX (homeobox A, C, D) gene

HOX family participates in patterning (51). Genes in HOX cluster (*HOXA-D*) engage in controlling the lower limb axis development. Members of HOXD cluster, *HOXD12* and *HOXD13* were found to be involved in the development of TEV (52). Transmission defects in HOXA and HOXD apoptosis gene cluster were also found in TEV (53). Moreover, microdeletion of the 5' region of *HOXC* is also found to be a contributing factor in the development of both vertical talus and TEV (54).

Filamin B (*FLNB*)

FLNB is a cytoplasmic protein that regulates intracellular communication and signaling by cross-linking the protein actin and thus allows direct communication between the cell membrane and cytoskeletal network, thereby controlling and guiding proper skeletal development. *FLNB* mutation may lead to boomerang dysplasia atelosteogenesis I and III and Larsen syndrome (55,56,57,58). Although mutation in filamin B can cause a complex syndrome but three novel missense mutations in this gene were established in the development of TEV (59). A deletion in *FLNB E1792del* is also documented in isolated club foot patients (60).

COL9A1

Type IX collagen proteins are produced by *COL9A1* gene, which helps in strengthening the connective tis-

ues, ligaments, tendon, cartilage, bone, and skin (61). A study on the Chinese population showed that *COL9A1* rs35470562 variant may contribute to the development of the TEV (62). Liu et al demonstrated the high expression of a protein from *COL9A1* gene located on the rs1135056 encoding region may increase the susceptibility to develop TEV (63).

DISCUSSION

Recently mutations in several candidate genes or SNPs have been hypothesized to be involved in the molecular genetic basis of the TEV, but the main mechanism remains elusive (10,64,65). TEV inheritance among heterogenic families shows that it is associated with multiple genetic factors. These genetic factors and their regulatory sequences are further influenced by a few environmental factors making their discovery more complicated. To know the common denominator a neurovascular hypothesis has been proposed. Spinal anomalies and spina bifida frequently seen in the TEV deformities are suggested to be associated with neurodegenerative disorders (66,67). A study on sciatic nerve defect in the chicken and mice model of TEV phenotype found that upregulation of *LIMK1* gene causes peroneal muscular atrophy (68). Vascular insufficiencies and occlusion of vascular tree at Sinus tarsi canal of the ankle and foot is found in limbs of patients affected by TEV (69,70). The finding of joint laxity in TEV patients supports the theory of connective tissue defect (68). Calcaneus and talus bone anomalies with reduced fetal movement also support the concept of physiological deformity of the foot (1,71). All these mechanisms for the development of TEV are related to the genes which are key players in the cytoskeleton formation. A healthy and genetically maintained cytoskeleton of feet during intrauterine life is important for the maturity of feet. Any disruption in the physical property or shape of the cytoskeleton of bones, muscles, ligaments, and soft tissues may lead to deformed foot.

Since its description by Hippocrates in 400BC, search for its possible causes was started. Data on segregation analysis suggested the "major genes" involved in the development of TEV. However, because of heterogeneity of the genetic causes the candidate gene approach has failed to reveal the exact number of causative variants in both isolated and syndromic TEV phenotypes. Moreover, Sadler et al classified the genetics of isolated and syndromic club foot and concluded that *FLNB* is involved in both types (72). As shown in table 2 genes involved in the club foot are also involved in the other

Table 1. The most common genes involved in the development of TEV.

Genes	Associated with other phenotype	References
<i>PITX- gene</i>	Orofacial clefts	39,40,41,42, 43,44,45
	Developmental hip dysplasia	
	Patella hypoplasia, Tibial hemimelia,	
	Preaxial polydactyly	
<i>TBX4- gene</i>	Skeletal dysplasia	46,47,48
	Pulmonary hypertension	
	Coxodopattellar syndrome Amelia	
<i>HOX A</i>	Severe limb and genital abnormalities.	52,53,54
<i>FLNB</i>	Dysplasia atelosteogenesis I and III and Larsen syndrome	55,56,57,58,60
<i>COL9A1</i>	Osteoarthritis	61,62,63
	Epiphyseal dysplasia, Stickler syndrome	

disease processes. Studies published on the management of club foot mentioned additional features appear even after doing surgical intervention in the clubfoot patients during their adulthood. (73). Case reported by Milenkovic. et al in a 56 year of age suggesting additional feature like degenerative changes in the hindfoot and thoracolumbar scoliosis with degenerative spondyloarthrosis in thoracolumbar spine segments (74). Sequencing analysis in one study failed to detect genetic variants in *TBX4*, *PITX1*, *HOXD12*, and *HOXD9* in two Pakistani families (75). They suggested that mutations may be present at the regulatory region of these genes. The literature review on a good number of studies proved that relapse of the disease process occurs even after corrective surgery because of tissue deposition indicating that pathobiological factors do persist and keep on causing the issues (76,77).

Recently more advanced techniques became available to get a promising result for the underlying cause of TEV. Among all the reported genetic studies using different techniques, the next generation sequencing (NGS) including whole genome sequencing and whole exome sequencing (WES) are getting popularity in common clinical diagnosis as well as in research on gene identification in inherited diseases. To get the most effective results it is useful to use the combination of these techniques with linkage analysis (78).

CONCLUSION

TEV is a multifactorial condition with genetic disruption of multiple molecules in the cytoskeleton effected by the exposure to adverse environmental factors as well as to genetic factors. The available literature shows deficit in high profile studies as many studies focusing on the genetic causes of this deformity lacked speculating harmony in proving exact genetic cause in both isolated and syndromic types of talipes equinovarus. Therefore, refinement of the existing genes of isolated clubfoot and clubfoot-associated phenotypes in early and late adulthood will lead to more effective genotype determination and it will improve the diagnostic capabilities and management options. Hence, large multiscale, multicenter collaborative studies using genetic techniques like GWAS with SNP scan for linkage analysis are required on families affected with TEV. Furthermore, inheritance pattern and penetrance will help to skim through novel genes involved in this disorder. Discovery of the genetic factors will revolutionize the management of the TEV and can eliminate the disability of the patients that often persists.

Nonetheless, we would like to put forward the hypothesis however that genes found to be implicated in club foot do not only cause club foot but will lead to multiple symptoms and the affected patients are suffering from syndromic club foot. So, we need to thoroughly investigate the affected individuals for the possibility of other syndromes. In other words, the classification of club foot into isolated and syndromic club foot needs to be revised.

AUTHOR CONTRIBUTIONS

Yasir Naseem khan wrote the initial draft of the article under the supervision of Mohammad Imad. Mohammad Imad has reviewed and suggested, and changes required for publications. Both authors contributed to and have approved the final article.

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A study of acromion morphology and morphometry in north indian population and its significance in subacromial impingement syndrome and rotator cuff tears

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Abstract. *Introduction.* The acromion process serves as a point of attachment for various muscles and ligaments and is a pivotal factor in the development of shoulder impingement syndrome and rotator cuff pathology. The study aims to evaluate the acromion process of dry human scapulae in residents of North India and understand the implications of these in relation to shoulder impingement syndrome and rotator cuff pathology. *Material and Methods.* The present study comprised of 100 adult scapulae of unknown sex obtained from Department of Anatomy, Government Medical College, Amritsar. The acromion process was studied for shape of tip of acromion, inferior surface, enthesophytes, os acromiale, acromial facet, maximum length, width, anterior thickness, distance between tip of acromion and coracoid. *Results.* The most common shape of tip was found to be intermediate. The most common shape of acromial facet observed was oval and it was more medially inclined. The inferior surface of acromion was rough in 79% bones. Enthesophytes were found in 16 bones which were more common in type II acromion and right side. Width, Length, Anterior Thickness, distance between tip of acromion and coracoid was found to be less on left side as compared to the right side. *Discussion.* The majority of the parameters were observed to be higher on the right side which proved to be significant for orthopedicians. Facts about the common variant and morphometric proportions of acromion process can support to improve understanding and preparation for the treatment of rotator cuff pathology due to the impingement syndrome.

Keywords: acromion, shoulder pain, shoulder impingement syndrome, subacromial impingement syndrome.

INTRODUCTION

The acromion process is a bony projection or extension of the scapula, the shoulder blade. Being a prominent feature of the scapula, it plays significant role in the structure and function of the shoulder joint. It forms the outermost part of the shoulder blade and is easily palpable at the top of the shoulder. It articulates with the clavicle (collarbone) to form the acromioclavicular joint, which is important for the movement and stability of the shoulder. The acromion also provides attachment points for the deltoid muscle, which is a major muscle responsible for lifting and revolving the arm, as well as other muscles and ligaments that are involved in shoulder movement and stability. Different shapes of the acromion are associated with a variety of pathologies such as impingement syndrome and rotator cuff tear.¹

Shoulder pain is a disabling symptom frequently encountered in patients of shoulder complaints. The estimated prevalence of shoulder complaints is 7–34%. One of the most common diagnosed shoulder disorder is Shoulder impingement syndrome(SIS) causing chronic shoulder pain. Its incidence ranges from 36% to 74% of patients of shoulder complaints.

In simple terms, SIS can be defined as a collection of shoulder symptoms and signs caused by pathology within the rotator cuff tendon itself (intrinsic) or structures external to it (extrinsic), causing impingement in the tapering space between the acromion and humeral head.⁴ This syndrome, if left untreated, could result in rotator cuff disruption which then persists to cause secondary osteoarthritis of the shoulder, severely restricting shoulder movement in the end.⁵

As for now, there has not been a clear demonstration of SIS pathogenesis. There are 2 proposed mechanisms i.e intrinsic and extrinsic mechanism.⁶ In the extrinsic mechanism, acromion is one of the structures involved in causing SAIS. Thus, the morphology and other parameters of the acromion are interesting to study. Dry bone measurement is more cost-effective when compared to imaging study. The variations of acromial morphology are different among races. Thus, it is important to study dry bone for the morphology of acromion in north Indian population and using it to correlate with SIS.

AIM

Aim of the study is to determine the morphology of acromion process of scapula in North Indian population and to find the association with subacromial impingement syndrome and rotator cuff pathology.

MATERIAL & METHODS

The material for the present study comprised of 100 adult scapulae of unknown sex, obtained from Department of Anatomy, Government Medical College, Amritsar. These scapulae were thoroughly cleaned and boiled. These non pathological scapulae were free from any physical deformity or abrasion and were complete in all respects i.e. the upper and the lower ends were intact, so as to give the correct measurements. They were labelled from 1-100 with suffix R (Right) or L (Left). Different morphological features were observed and morphometric measurements were taken. Both sides scapulae were inspected to describe anatomical morphology and data were recorded. The following parameters were studied:

1. Acromion process:

- a) Shape of tip of acromion: whether cobra shaped, square shaped or intermediate type^{8,9}.
- b) Acromial facet of acromioclavicular joint:
 - i. Shape: oval or other.
 - ii. Inclination: medially, vertically or laterally inclined^{10,11}.



Fig. 1

AB.: vertical diameter of acromial facet

CD.: transverse diameter of acromial facet

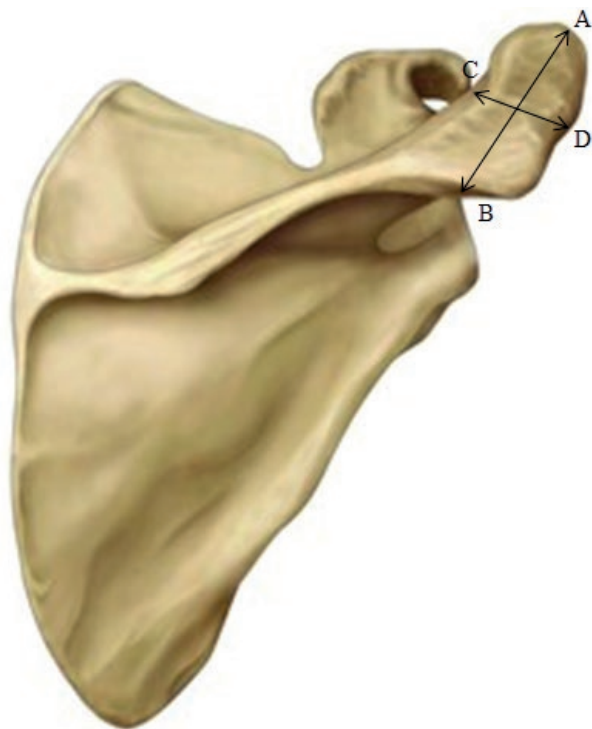


Fig 2

AB : maximum length of acromion process

CD : maximum breadth of acromion process

- iii. Vertical diameter: It was measured from mid-point of its upper border to that of the lower border with the help of vernier calipers (AB in Fig. 1).
- iv. Transverse diameter: It was measured from its anterior end to the posterior end with the help of vernier calipers (CD in Fig. 1).
- c) Inferior surface:
 - i. Rough / smooth: It was observed whether inferior surface was rough or smooth^{10,11}.
 - ii. Shape: Its shape was observed whether flat, curved, hooked or convex^{10,11} and on the basis of shape of inferior surface, the acromion process was classified type I (flat), type II (curved), type III (hooked) or type IV (convex)^{12,13}.
 - iii. Enthesophytes (also called as acromion spur by Nicholson et al.)¹⁸: The acromion process was observed for presence or absence of enthesophytes¹⁰.
- d) Os acromiale : An attempt was made to find out os acromiale which is a clean, linear joint horizontal to the axis of acromion.



Fig. 3

AB : Maximum distance between acromion coracoid

AC : Maximum distance between acromion coracoid

- e) Maximum length: It was measured from the tip to the lower border of the crest of the spine in its mid sagittal plane^{10,11} with the help of vernier calipers (AB in Fig. 2).
- f) Maximum width: It was measured with the vernier calipers as the distance between the lateral and medial borders at the mid point of acromioclavicular ligament insertion^{10,11} (CD in Fig. 2).
- g) Anterior thickness: It was measured with the vernier calipers as the maximum thickness of the acromion^{15,16}.
- h) Maximum distance acromion coracoid: It was measured with the vernier calipers as the distance between the tip of the acromion and the coracoid tip^{14,15}. (AB in Fig.3) and between the tip of the acromion and mid point of lateral border of coracoid^{12,17} (AC in Fig. 3).

RESULTS

1. Acromion process

- a) Shape of tip of acromion : The most common shape of tip of acromion was found to be intermediate in 42(42%) bones whereas it was cobra shaped in 38 (38%) and square shaped in 20 (20%) bones. The incidence of intermediate type was equal for both right and left sides i.e 21 bones (21%). Cobra shape was more predominant on right side seen in 22 bones (44%) whereas square shape was more predominant on left side seen in 13 bones (26%) (Table 1).
- b) Acromial facet of acromioclavicular joint
- Inclination of acromial facet : Out of the 93 bones having acromial facet, in 74 bones (79.60%) the facet was medially inclined. Incidence of medial inclination was much more on the right side 43(93.48%) as compared to the left side 31(65.96%). On the left side, vertical inclination is more prevalent [11(23.40%)] as compared with right side [1(2.17%)] (Table 1).
 - The mean vertical diameter of acromial facet for right and left side were 7.14mm (Range=4.35-11.67mm) and 7.24mm (Range=4.35-12.97mm) respectively (Table 2).
 - The mean transverse diameter of the facet for right and left side were 12.77mm (Range=16.68-29.98mm) and 12.74mm (Range=15.63-29.26mm) respectively (Table 2).
- c) Inferior surface
- It was rough in 79 (79%) bones and smooth in 21 (21%) bones. The corresponding figures on the right side were 36 (52%) and 14 (28%); and

on the left side were 43 (86%) and 7 (14%) for rough and smooth respectively (Table 1).

- Out of the 100 bones of the present study, the shape/type was found to be curved in 43 (43%), flat in 31 (31%), convex in 15 (15%) and hooked in 11 (11%) bones. The commonest type was the curved on both right and left sides (Table 1).
- Type II was the most observed type in 43% bones. Type I was next (31%), type IV (15%) and type III least common (11%) (Table 1).
- Enthesophytes: the enthesophytes (also termed as acromial spur by Nicholson et al.)¹⁸ were present in 16 (16%) bones out of 100 bones. Out of these, 10 (20%) bones belonged to the right side and 6 (12%) belonged to the left side. As far as association between the enthesophyte formation and type of acromion is concerned, out of the 16 bones with enthesophytes, 7 (43.75%) were of type II, 5 (31.25%) were of type III, 2 (12.5%) each were of type I and IV. Thus type II and III are more prone to enthesophyte formation. Neer²⁰ was the first to suggest that enthesophytes protrude into the subacromial space causing subacromial impingement and rotator cuff tears. These tears may be primary, initiated by intrinsic degenerative tendinopathy, and this incompetent cuff allows a proximal humeral migration with increased tension on the ligament that causes the growth of enthesophytes and impingement. Nicholson et al.¹⁸ reported that traction spurs may develop over time, especially if an incompetent rotator cuff allows proximal humeral

Table 1. Comparison of morphology of acromion process in right and left side of scapula

Parameters		Right(n=50)	Left (n=50)	Total(n=100)
Shape(Tip of Acromion)	Cobra	22(44%)	16(32%)	38(38%)
	Square	7(14%)	13(26%)	20(20%)
	Intermediate	21(42%)	21(42%)	42(42%)
Inclination	Medial	43(93.48%)	31(65.96%)	74(79.60%)
	Vertical	1(2.17%)	11(23.40%)	12(12.90%)
	Lateral	2(4.35%)	5(10.64%)	7(7.53%)
Inferior surface	Rough	36 (52%)	43 (86%)	79 (79%)
	Smooth	14 (28%)	7 (14%)	21 (21%)
	Prevalence in type	TypeII (44.44%)	TypeII (46.51%)	TypeII (45.60%)
Shape/Type	Flat (type I)	13 (26%)	18 (36%)	31 (31%)
	Curved (type II)	21 (42%)	22 (44%)	43 (43%)
	Hooked (type III)	6 (12%)	5 (10%)	11 (11%)
	Convex (type IV)	10 (20%)	5 (10%)	15 (15%)

migration with increased contact on the ligament. These spurs may then contribute to impingement and may be a factor in continuing tendon wear and damage.

- d) Os acromiale: although its existence has been reported by many authors, it was found to be absent in present bones.
- e) The mean maximum length of acromion process observed was 44.10 mm (Range = 23.66-55.26 mm). On the right side, it was 45.57 mm (Range=23.78-54.61 mm) whereas on the left side, it was 42.64 mm (Range=23.66-55.26 mm). Thus it was higher on the right side than the left side (Table 2).
- f) The mean width of acromion on the right side was 23.68mm (Range=16.68-29.98mm) whereas on the left side, it was 22.82mm (Range=15.63-29.26mm) (Table 2).
- g) The mean anterior thickness of acromion on the right side was 7.41mm (Range=4.95-10.52mm) whereas on the left side, it was 7.04mm (Range=4.67-9.97mm) (Table 2).
- h) The mean value of distance between tip of acromion and tip of coracoid on the right side was 38.56mm (Range=26.25-68.10mm) whereas on the left side, it was 38.15mm (Range=22.97-56.96mm). The mean value of distance between tip of acromion and lateral border of coracoid was 31.72mm (Range=15.82-59.36mm). On the right side, the value was observed to be 31.91mm (Range=22.17-59.36mm) whereas on the left side, it was 31.54mm (Range=15.82-47.14mm) (Table 2) .

DISCUSSION

The morphology of the acromion is assumed to be related to pathology of the rotator cuff and other shoulder impairments. Earlier Nicholson et al.¹⁸ and Paraskevas et al.¹⁰ have studied the inclination of acromial facet. While Nicholson et al.¹⁸ found it to be almost equally distributed between 2 types (medial and vertical inclination), Paraskevas et al.¹⁰ found medial inclination to be more prevalent. In our study, it was found to be more medially inclined (Table 3).

Earlier many authors have studied the shape of the inferior surface of the acromion. A vis a vis comparison with them has depicted that curved type is the most prevalent in almost all the studies done earlier in accordance with our study in which curved is found to be the most prevalent type (Table 4).

Neer¹⁹ and Nicholson et al.¹⁸ were of the opinion that the undersurface of the anterior 1/3 of the acromion is under the influence of coracoacromial ligament resulting in the formation of different acromial types. Wang et al.²⁰ are of the view that the acromial shape has a strong correlation with the severity of symptoms in impingement syndrome and it influences the outcome of conservative therapy. Natsis et al.¹³ blamed hooked (Type III) acromions for shoulder impingement syndrome and rotator cuff tears. Farley et al.²² confirmed this, but stressed that acromioplasty in patients with this type of acromion should include the mid portion of the acromion to achieve the anticipated decompression of the subacromial space. It is commonly accepted that rotator cuff lesions are noticed mainly in the hooked acro-

Table 2. Comparison of Morphometric parameters of Acromion process in right and left side scapula.

Parameters	Mean (mm)		Range (mm)		
	Right (n=50)	Left (n=50)	Right	Left	
Diameter of Acromial Facet	Vertical	7.14	7.19	4.35-12.97	4.35-12.97
	Transverse	12.77	12.75	15.63-29.98	15.63-29.98
	Width	23.68	23.25	16.68-29.98	15.63-29.26
Acromion Process	Length	45.57	44.10	23.66-55.26	23.66-55.26
	Anterior Thickness	7.41	7.23	4.67-10.52	4.67-9.97
Distance between tip of acromion and tip of coracoid	38.56	38.36	22.97-68.10	22.97-68.10	
Distance Between tip of acromion and lateral border of coracoid	31.91	31.72	15.82-59.36	15.82-59.36	
			22.17-59.36	15.82-47.14	

Table 3. Showing comparison of various parameters of Acromion process.

Author	Von				Coskun et al. ⁸		Present Study	
	Nicholson et al. ¹⁸	Gallino et al. ¹⁶	Paraskevas et al. ¹⁰	Schroeder et al. ¹²	Piyawinijwong et al. ¹⁴	Right	Left	
Population (n)	American (396)	Egyptian (266)	Greek (88)	Canadian (30)	Thai(97)	Turkish (90)	North Indian (100)	
Shape of tip								
Inclination of acromial facet	M 49 L 48 3	M 46 V 38 L 4	M 46 V 38 L 4			C 28(31%) S 12(13%) I 5(56%)	C 38(38%) S 20(20%) V 7(14%) L 13(26%)	I 42(42%) L 21(42%)
Length	44.55	41.5	46.1	48.0	40.0	44.7	44.1	42.64
Breadth	18.95		22.3	21.9	23.9		23.25	22.82
Anterior thickness	7.2	6.9	8.8	9.4	6.4		7.23	7.04
Maximum distance between tip of acromion and tip of coracoid		27.4			29.5		38.36	38.15
Maximum distance between tip of acromion and lateral border of coracoid		28.1	27.1				31.72	31.54

Table 4. Showing comparison of shape and type of inferior surface of acromion.

Author	Race (n)	Shape/Type			
		Flat (I)	Curved (II)	Hooked (III)	Convex (IV)
Nicholson et al ¹⁸	American(396)	127 (32%)	165 (42%)	104 (26%)	-
Gallino et al ¹⁶	Egyptian(233)	48(20.6%)	169(72.5%)	16 (6.9%)	-
Gumina et al ¹⁹	Italian(204)	45%	34%	21%	-
Von Schroeder et al ¹¹	Canadian(30)	23%	63%	14%	-
Coskun et al ⁸	Turkish(90)	9 (10%)	66 (73%)	15 (17%)	-
Natsis et al ¹³	German(423)	51 (32%)	239(56.5%)	122(28.8%)	11 (2.6%)
Paraskevas et al ¹⁰	Greek(88)	23 (26.1%)	49 (55.6%)	16 (18.1%)	-
Present study	North Indian(100)	13 (26%)	21 (42%)	6 (12%)	10 (20%)
		18 (36%)	22 (44%)	5 (10%)	5 (10%)
		31 (31%)	43 (43%)	11 (11%)	15 (15%)

mion. Nicholson et al.¹⁸ explained this correlation by the reduction in the dimensions of the subacromial space in the hooked acromion, which more often leads to impingement of the rotator cuff. However, they lamented that it is still open to question whether the hooked shape is a congenital feature or represents a degenerative change by which type I is converted to type III in the course of time.

Out of the 100 bones of the present study, when compared on both the sides, the length was more on right side as compared to the left side. On comparing both the sides, the mean width was more on the right side as compared to the left side. An increased length of acromion limits the overhead activities and is closely associated with degenerative changes. Similarly, increased dimensions are useful for supporting screw, pin or wire for fracture stabilization of acromioclavicular joint or arthrodesis of shoulder joint²³. There was negligible difference in the values of vertical and transverse diameter of the facet of the two sides. Our values were less than those found by Nicholson et al.¹⁸. The acromion was wider on the right side than on the left side. Acromial shape and dimensions are of particular importance in acromioplasty for rotator cuff impingement syndrome¹⁹. Earlier Nicholson et al.¹⁸, and Paraskevas et al.¹⁰ have measured this parameter in different populations. When we compare their results with the present study, it is evident that our values were near to those of in their population. The values for the right side were more than the left side (Table 3). When we compare our study with Paraskevas et al.¹⁰, our value was higher than those found by them. We observed that the mean value of distance tip of acromion between tip of coracoid and lateral border of coracoid was more on the right side than on the left side. Neer¹⁹ cautioned against excessive

resection while doing acromioplasty in open surgery in the races with thin acromion. It is further stressed by some authors that such precautions should also be exercised in the arthroscopic version of acromioplasty, which may not allow a precise estimate of the amount of resected acromion.

CONCLUSION

To conclude, it can be said that these findings of the present study abide by the results of previous authors but a racial variation was also observed in various dimensions. The majority of the parameters were observed to be higher on the right side than the left side. The differences between the present study and the other studies in these morphometric parameters show that there are racial and regional variations. This knowledge will be helpful for the orthopedicians in diagnosing and planning treatment procedures for patients with impingement syndrome and rotator cuff pathology.

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Upper limb arterial development theories used to explain arterial variations in adults

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Abstract. The formation of the upper limb arterial pattern takes place in several stages during the embryonic development. The arterial variations observed in the adult population are thought to occur during the developmental stages because of the primitive arteries failing to form or recede, as well as unusual origins of native vessels. Two contrasting theories of upper limb arterial development have been suggested, one by Singer, 1933 who suggested that the upper limb arteries develop from a single axial trunk, and the other by Rodriguez-Niedenfuhr et al., 2001 who suggested that the upper limb arteries develop from a capillary plexus. While the two theories describe the development process differently, the two theories are cited in an interchangeable manner, raising questions about which of the two theories is accepted as correct by the authors. This review seeks to record and compare the utilization of both theories. A literature search for articles and case reports between 2002 and 2022 was conducted, using several search engines, including ResearchGate, Google Scholar, PubMed, Medscape and Science Direct. 38 articles were used in this review. The chi-square test did not pick up any significant differences in the use of the two theories ($P=0.223$). We conclude that neither of the two theories is preferred by authors as they are almost equally cited. These results suggest that confusion remains as to which of the two theories is accepted. Further research on the upper limb arterial development is necessary to establish the accuracy of the two existing theories.

Keywords: embryonic, arterial development, arm, forearm.

INTRODUCTION

The development of the arterial pattern of the upper limb is said to arise during several embryonic stages. The seventh intersegmental artery gives rise to a single axial artery, which then gives rise to the arteries of the upper limbs (DeSesso, 2017). According to Singer, 1933, the upper limb arteries arise from a single axial artery, which represents the brachial and interosseous arteries (Singer, 1933) (Fig. 1). However, the above description by Singer, 1933 was not based on his own study but rather on the study conducted by Senior, 1926. Nonetheless, this theory is still commonly known as Singer's (1933) theory in literature to date. Contrary to Singer's (1933) theory of a single axial arterial trunk, a study by Rodriguez-Niedenfuhr et al., 2001 utilised 112 human

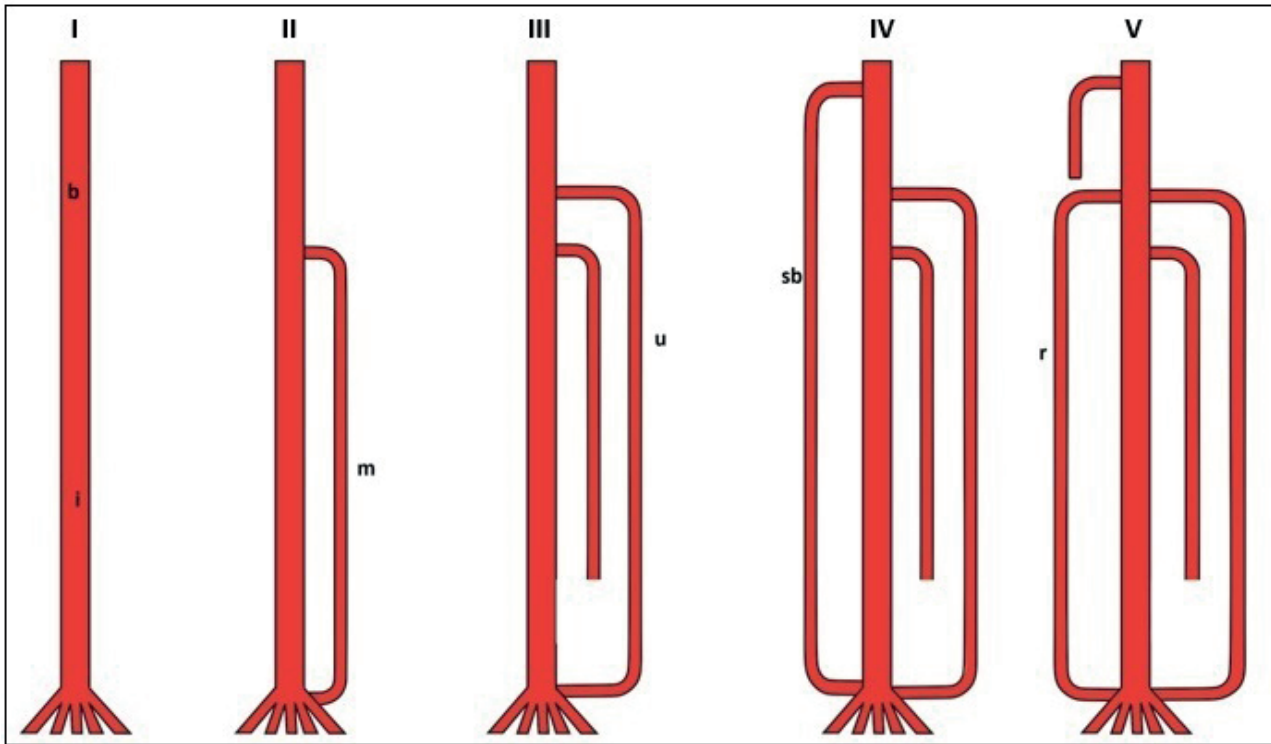


Figure 1. An illustrative diagram showing the theory of the embryonic development of the upper limb arterial pattern proposed by Singer, 1933 (Adapted from Rodriguez-Niedenfuhr et al., 2003).

embryos and concluded that the upper limb arteries arise as an initial capillary plexus from the dorsal aorta during the 12th embryonic stage (26–30 days) of development (Fig. 2). The definite arteries of the upper limb arise from stage 14 (31–35 days), starting with the subclavian artery through to stage 23 (56–60 days), where the radial artery is completely defined. The above authors challenged Singer's (1933) theory as it was based on data from a previous study by Senior, 1926, without the consideration of embryonic material (Rodríguez-Niedenfuhr et al., 2001, Rodríguez-Niedenfuhr et al., 2003). Additionally, Rodríguez-Niedenfuhr et al., 2001 argued that the theory proposed by Singer, 1933 was limited as it was able to explain those cases in which the radial artery originated above the elbow level but was unable to explain other variations like an ulnar artery arising above the elbow level. In agreement with Rodríguez-Niedenfuhr's et al. 2001 theory, another study showed that an early anterior limb bud receives vascular supply from the fifth to the ninth pairs of cervical intersegmental arteries that arise from the aorta (DeSesso, 2017). The above authors noted that the seventh cervical intersegmental artery persists for the development of the upper limb arteries.

Currently, there seems to be no consensus in the literature regarding which of the above two theories (Sing-

er, 1933 and Rodríguez-Niedenfuhr et al., 2001) is most accepted as authors quote one or the other. In addition, very few studies have been done on the embryos to support or dispute the above two theories of upper limb arterial development, with most of the studies simply referring to a few available previous studies. Knowledge of the upper limb arterial development is crucial as the variations observed in the adults are thought to occur during the developmental stages due to unusual origins of native vessels or primitive arteries failing to form or recede (Ciervo et al., 2001, Chrysoglou et al., 2022). This review seeks to record and compare the use of the two upper limb arterial development theories to establish which one is most accepted by most of the authors as accurate. This information will help to establish the common ground in explaining the upper limb arterial variations observed during surgical procedures and inform the direction of future research on the subject.

MATERIALS AND METHODS

A literature search for articles and case reports between the years 2002 and 2022, describing the developmental basis of the variations observed in the upper limb

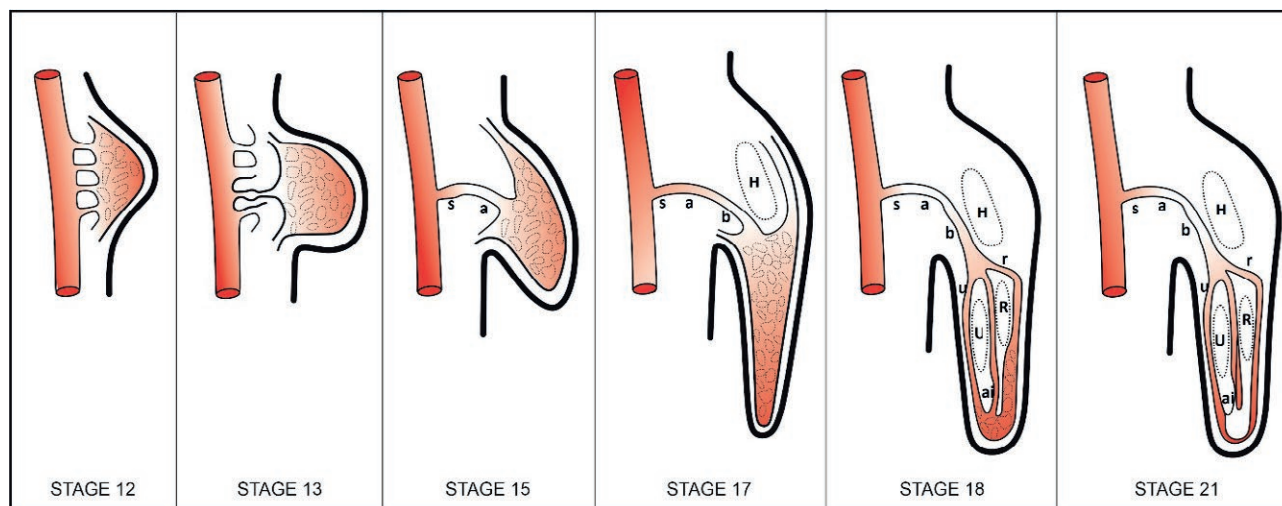


Figure 2. An illustrative diagram showing the theory of the embryonic development of the upper limb arterial pattern proposed by Rodriguez-Niedenfuhr et al., 2001 (Adapted from Rodriguez-Niedenfuhr et al., 2003).

arteries, was conducted. A total of thirty-eight (n=38) articles were used in the current review. The keywords for search included variations of the axillary artery, brachial artery, radial artery, and ulnar artery. The search engines included: (i) ResearchGate, (ii) Google Scholar (iii) PubMed (iv) Medscape and, (v) Science Direct. The references from the articles were assessed to find other relevant articles. Articles describing upper limb arterial variations with a description of the embryonic development were included, while those articles describing upper limb arterial variations without a description of the embryonic development were excluding.

RESULTS

Variations of the axillary artery and their embryonic developmental basis

Variations of the axillary artery accounted for 34,15% of upper limb arterial variations in this literature search. The most variable branch of the axillary artery is the subscapular artery. The variabilities of the subscapular artery include trunk formations with other branches and origin from the second instead of the third part of the axillary artery. The most encountered trunk formation is the common trunk of the subscapular artery and the lateral thoracic artery. The above variation was recorded in six of the 11 articles that reported the variations of the axillary artery in the current review (Sreeja and Leo Rathinaraj, 2014, Singh et al., 2020, Tiwari and Afroze, 2020, Chakraborty and

Sarkar, 2019, Ovhal et al., 2021, Yang et al., 2021). All six authors described this variation as arising from either the persistence, enlargement or differentiation of certain branches of the capillary plexus in accordance with Rodriguez-Niedenfuhr's et al., 2001 theory. The remaining five of the eleven authors recorded arterial trunks, which included a common trunk from which the subscapular, anterior and posterior circumflex humeral arteries arise from and a common trunk from which the subscapular and posterior circumflex humeral arteries arise from (Ovhal et al., 2021, Yang et al., 2021, Astik and Dave, 2012, Singh, 2017, Padmalatha et al., 2018). All five of the above authors described the common trunk for the subscapular, anterior and posterior circumflex humeral arteries and the common trunk for the subscapular and posterior circumflex humeral arteries as arising from the unusual pathways that embryonic vessels follow, or the failure of capillaries from the primitive capillary plexus to form or recede as they should, in accordance with Rodriguez-Niedenfuhr's et al., 2001 theory. One of the above authors (Padmalatha et al., 2018) used Singer's (1933) illustrations while describing the trunk formation according to Rodriguez-Niedenfuhr's et al., 2001 theory in explaining the embryonic basis of these trunk formations, adding to the confusion of the acceptance of one or the other of the two theories. Two authors (Naveen et al., 2014, Saeed et al., 2002) described the two trunks to be due to the sprouting of vessels at unusual locations, as well as the persistence of sprouted vessels that are meant to regress in accordance with Singer's (1933) theory.

Variations of the brachial artery and their embryonic developmental basis

The variations of the brachial artery include high bifurcation, superficial and accessory brachial arteries.

The high bifurcation of the brachial artery is when this artery bifurcates into its terminal branches proximal to the level of the intercondylar line (Tsoucalas et al., 2020). This variation of the brachial artery has an incidence of 14,63%. Six authors reported on the high bifurcation of the brachial artery and the basis of its embryonic development (Kumar and Rathnakar, 2014, Mehta et al., 2008, Deka, 2018, Balasubramanian et al., 2018, Jadhav and Pawar, 2018, Sophia et al., 2021). Three of the above six authors (Mehta et al., 2008, Deka, 2018, Balasubramanian et al., 2018) described this variation as the sprouting of the terminal branches of the brachial artery at a level higher than the usual point of sprouting, resulting in the high bifurcation of the brachial artery, in line with Singer, 1933. However, one of the above three authors (Balasubramanian et al., 2018), while using Singer's (1933) theory to describe the high bifurcation of the brachial artery utilised Rodriguez-Niedenfuhr's et al., 2001 illustrations, which is contrary to Singer's (1933) theory as it depicts the basis of development arising as a capillary plexus which undergoes elongation and differentiation in the limb bud as opposed to the sprouting process from the axial artery described by Singer, 1933. As explained above, the combination of the two theories by the authors poses a contradiction as the two theories differ in explaining the upper limb arterial pattern of development. Three of the six authors (Kumar and Rathnakar, 2014, Jadhav and Pawar, 2018, Sophia et al., 2021) described the high bifurcation of the brachial artery as the persistence of the proximal part of the radial artery and the failure of an established connection with the brachial artery at the level of the ulnar artery, resulting in the high bifurcation of the brachial artery in line with Rodriguez-Niedenfuhr et al., 2001. Two of the abovementioned six authors (Kumar and Rathnakar, 2014, Sophia et al., 2021) described the high bifurcation according to Singer, 1933 but cited Rodriguez-Niedenfuhr et al., 2001, while one author (Jadhav and Pawar, 2018) cited Rodriguez-Niedenfuhr et al., 2001. However, the description of the actual developmental process was that of Singer, 1933 for all of the abovementioned six authors.

Superficial brachial artery

The superficial brachial artery is a brachial artery that runs superficial to the median nerve instead of run-

ning deep to this nerve (Sharma et al., 2009, Shetty et al., 2022). This variation has an incidence of 12, 20%. It was reported by five authors (Sharma et al., 2009, Nkomozezi et al., 2017, Kachlik et al., 2011a, Lalit and Piplani, 2021, Yang et al., 2008). The abovementioned authors suggested that under normal developmental circumstances, the brachial artery that passes deep into the median nerve is given hemodynamic preference over the one passing superficially to the median nerve, as it becomes obliterated at a later stage. However, in the case of the persistent superficial brachial artery, in accordance with Singer's (1933) theory, this artery receives hemodynamic preference, and the deep brachial artery gets obliterated instead. While all five authors described the variation in accordance with Singer's (1933) theory, two of the five (Kachlik et al., 2011a, Lalit and Piplani, 2021) stated and quoted Rodriguez-Niedenfuhr et al., 2001 while using Singer's (1933) theory to describe the variation.

Accessory brachial artery

The accessory brachial artery is a rare variant artery which originates from the brachial artery in the upper one third of the arm and, in some cases, from the axillary artery with an incidence of 7,32% (Kachlik et al., 2011b). The accessory brachial artery rejoins the brachial artery before it bifurcates in the cubital fossa into the ulnar and radial arteries (Kachlik et al., 2011b). Three authors reported the accessory brachial artery (Kachlik et al., 2011b, Elnaiem et al., 2022, Chakravarthi et al., 2014). The above authors described the accessory brachial artery as sprouting from the superficial brachial artery, which is also a vestigial artery as described above. Furthermore, it was suggested that on some occasions, this variation may arise due to the persistence of another cervical intersegmental artery in addition to the persisting seventh cervical intersegmental artery. Two of the above three authors (Chakravarthi et al., 2014, Elnaiem et al., 2022) who described the accessory brachial artery, based their descriptions on Singer's (1933) theory, while one author (Kachlik et al., 2011b) based the description on Rodriguez-Niedenfuhr's et al., 2001 theory.

High origin of radial artery and its embryonic developmental basis

A high origin radial artery is one that originates proximal to its usual point of origin in the cubital fossa from either the axillary artery or from the brachial artery in the upper part of the arm (Rodriguez-

Baeza et al., 1995). This high origin of radial artery has an incidence of 19,51%. Eight authors reported on the high origin of the radial artery (Pelin et al., 2006, Konarik et al., 2009, Shiny Vinila et al., 2013, Gandhi and Lakshmi, Ghosh and Chaudhury, 2018, Nasr, 2012, Klimek-Piotrowska et al., 2013, Haładaj et al., 2018). Seven of the above eight authors (Pelin et al., 2006, Konarik et al., 2009, Shiny Vinila et al., 2013, Gandhi and Lakshmi, Ghosh and Chaudhury, 2018, Nasr, 2012, Klimek-Piotrowska et al., 2013) described this variation as arising because of non-regression of the proximal part of the superficial brachial artery. During development, the distal part of the superficial brachial artery gives rise to the radial artery, while the proximal part undergoes regression. Failure of this regression results in the radial artery arising from the proximal part of the embryonic superficial brachial artery instead of the distal part and, therefore, adopting a high origin in accordance with Singer's (1933) theory. However, three of the above authors (Gandhi and Lakshmi, Ghosh and Chaudhury, 2018, Klimek-Piotrowska et al., 2013) cited Rodriguez-Niedenfuhr et al., 2001, despite using Singer's (1933) theory. One of the above authors (Haładaj et al., 2018) described this variation using both theories, firstly as arising due to the selective differentiation and remodelling process that the primitive plexus undergoes in accordance with Rodriguez-Niedenfuhr et al., 2001, and secondly, due to the persistence of the connection between the proximal part of the superficial brachial artery and the axial artery in accordance with Singer's (1933) theory.

High origin of ulnar artery and its embryonic developmental basis

A high origin of the ulnar artery has an incidence of 12,20%. Five authors reported on the high origin of the ulnar artery in the current review (Vollala et al., 2011, Krishnamurthy et al., 2006, Bhat et al., 2008, Bozer et al., 2004, Ghosh et al., 2016). Three of the above five authors described this variation as occurring due to an establishment of a connection between the ulnar artery and the axial artery in the arm proximal to the usual point of connection of the ulnar artery and the axial artery (Vollala et al., 2011, Krishnamurthy et al., 2006, Ghosh et al., 2016). The above authors further suggested that hemodynamic preference of the ulnar artery origin given to the superficial over the deep arterial system results in the persistence of embryonic vessels as described by Singer, 1933. While two of the above authors (Bhat et al., 2008, Bozer et al., 2004) described this variation to be due to one of the capillary buds from the

axillary artery persisting instead of following the proposed selective enlargement or regression of the primitive capillary plexus as described by Rodriguez-Niedenfuhr et al., 2001. While the above authors cited Rodriguez-Niedenfuhr et al., 2001, the embryonic description was that of Singer, 1933.

Table 1 summarises the upper limb arterial variations and the developmental theories used to describe the variations.

CONCLUSION

The chi-square statistical test did not pick any statistically significant difference in the number of authors who used either of the two theories ($P=0.223$). We conclude that none of the two theories is preferred over the other as the two theories are almost equally used in the literature. A small fraction of the authors used both theories, whereby the description of one theory was used but illustrated with the diagrams of the other theory, suggesting that the selection of one or the other theory is more of convenience than the belief in its correctness. It is also apparent that the majority of the authors used Rodriguez-Niedenfuhr's et al., 2001 theory to describe the variations of the axillary artery, while the majority of authors used Singer's (1933) theory to describe the variations of the brachial artery, further strengthening the idea of convenience than correctness in the selection of the use of the two theories. The equal use of the two theories illustrates the confusion around this subject, suggesting that more research is necessary for better scientific basis of the development of upper limb arteries. Such research can aid in explaining the multiple upper limb arterial variations observed and probably the prediction of the frequency of occurrence of specific ones for precautionary measures during surgery.

It is our suspicion that the scarcity of data around this subject could be due to ethical issues regarding the access to human embryos. More scientific debate on this subject and its ethical issues could help paving a way forward in further exploring the embryonic bases of arterial variations and racial differences in upper limbs arterial branching patterns.

AUTHOR CONTRIBUTIONS

Conceptualization: AT Sebelebele and NK Xhakaza. Drafting of the manuscript: AT Sebelebele. Critical revision of the manuscript: NK Xhakaza. Approval of the final version of the manuscript: Both authors.

Table 1. Summary of upper limb arterial variations and their description according to the two theories.

Arterial variations of the upper limb			
Variation	Author	Arterial development theory	
		Singer, 1933	Rodriguez-Niedenfuhr et al., 2001
Common Trunk for Subscapular Artery and Lateral Thoracic Artery	Sreeja and Leo Rathinaraj, 2014		×
	Singh et al., 2020		×
	Tiwari and Afroze, 2020		×
	Chakraborty and Sarkar, 2019		×
	Ovhal et al., 2021		×
	Yang et al., 2021		×
Subscapular-Bi-circumflex Humeral Trunk	Naveen et al., 2014	×	
	Yang et al., 2021		×
	Padmalatha et al., 2018	×	×
	Astik and Dave, 2012		×
Common Trunk for Subscapular Artery and Posterior Circumflex Humeral Artery	Singh, 2017		×
	Saeed, 2002	×	
	Ovhal et al., 2021		×
	Yang et al., 2021		×
High Bifurcation Brachial Artery	Kumar and Rathnakar, 2014		×
	Mehta et al., 2008	×	
	Deka, 2018	×	
	Balasubramanian et al., 2018	×	×
	Jadhav and Pawar, 2018	×	×
	Laishram et al., 2021		×
Superficial Brachial Artery	Lalit and Piplani, 2021	×	×
	Nkomozepe et al., 2017	×	
	Sharma et al., 2009	×	
	Yang et al., 2008	×	
	Kachlik et al., 2011	×	×
Accessory Brachial Artery	Chakravarthi et al., 2014	×	
	Kachlik, 2011		×
	Elnaiem et al., 2022	×	
High Origin Radial Artery	Pelin et al., 2006	×	
	Konarik et al., 2009	×	
	Shiny et al., 2013	×	
	Gandhi and Lakshmi, 2018	×	×
	Ghosh and Chaudhury, 2018	×	×
	Nasr, 2012	×	
	Klimek-Piotrowska et al., 2012	×	×
	Haladji et al., 2018	×	×
High Origin Ulnar Artery	Vollala et al., 2011	×	
	Krishnamurthy et al., 2006	×	
	Bhat et al., 2008		×
	Bozer et al., 2004		×
	Ghosh et al., 2016	×	

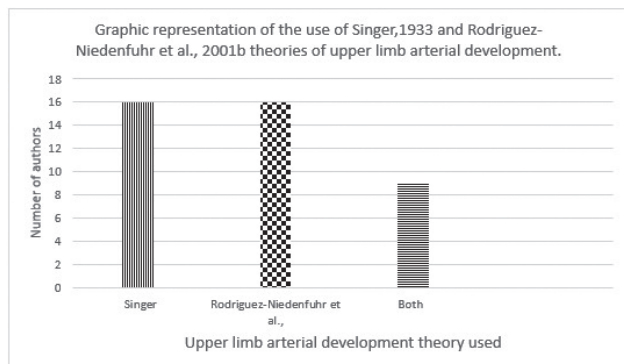


Figure 3. Graphic representation of the use of Singer, 1933 and Rodriguez-Niedenfuhr et al., 2001 theories of upper limb arterial development.

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Characteristics of a few observed variants of renal arteries, and their prehilary branching with kidneys morphometry

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Abstract. Human renal arteries are characterized by a wide range of variability. This study aimed to detect the variations of the renal arteries, make measurements in cadaveric samples and, based on a review of the literature, to compare results with those already published. *Materials and Methods.* At the Department of Morphology, kidneys of the formalin-fixed five cadavers were used for this study. Renal arteries and kidneys were explored, measured, and anatomical variations were noted. *Results.* Main renal arteries originated from the aorta, mainly at the L2 level. The right main renal arteries' mean length, diameter, and angle were 40.4 mm, 6.1 mm, and 75.6°, but the left - 32.2 mm, 6.0 mm, and 84.0°. The right accessory renal artery's mean length, diameter, and angle were 65.0 mm, 3.5 mm, and 115°, but left - 68.0 mm, 1.3 mm, and 74°. The mean length and width of the right kidney were 11.6 cm and 6.5 cm, and the left - 11.8 cm and 7.5 cm. The origins of the renal segmental arteries and prehilary branching patterns were variable. *Conclusions.* Detection of anatomy of the renal arteries may affect pathogenesis, clinical manifestations of various diseases, and the choice of methods of treatment.

Keywords: cadavers, kidney, renal artery, prehilary branching, variants.

1. INTRODUCTION

In the classical case, each kidney is supplied by a single renal artery, which arises as a lateral visceral branch of the abdominal aorta between the 1st and 2nd lumbar vertebrae levels. Related to the lumbar vertebra, the right main renal artery originates above the left renal artery. Determining any possible early branching of the main renal artery is essential. The pre-hilar or early branching pattern is a standard variant, and the main renal artery divides into segmental branches at a more proximal level than the renal hilum. Related to this, the component that diverges within 1.5 to 2.0 cm from the lateral wall of the aorta is named the pre-hilar branch [1].

In the kidney, the distribution of the arteries forms a unique pattern and division of the renal parenchyma into five segments (the apical, the upper (anterior), the middle (anterior), the lower and the posterior segment), where

every segment supplies its artery [2]. The first details of the renal pattern were described in the 1950s by Graves using the corrosion cast method [3]. The available literature data indicate that the investigation of renal artery variations prevalence is based on autopsy results [4].

Variations of renal arteries are seen more frequently than variations of renal veins [5]. Anatomical variation is defined as normal flexibility in the topography and morphology of body structures [6]. It differentiates from anomalies, abnormalities, and malformations commonly presented in the literature. Although the exact distinction between these terms has not been made, the latter should be applied when structural changes negatively influence body functions [7]. Variations may significantly influence predisposition to an illness, the course of a disease, the findings of clinical examinations, or patient management [8]. Knowledge of this type of anatomical variation of renal vascularization has etiological, diagnostic, and therapeutic importance [9].

The morphological aspect of this problem concerns the establishment of individual features and variants of anatomy, topography of the renal arteries, their quantitative and morphometric characteristics, spatial location, and sources of origin of the renal arteries.

Knowledge about variants and anomalies in the kidney's blood vessels is one of the essential tasks of morphology, as it represents a significant interest in practical medicine, which determines the relevance of such studies. In the past decade, researchers have provided a wealth of genetic and phenotypic information, questions, and tolls that are now well-defined. Still, despite this, a straightforward program of work for the next decade will lead to new insights into how the kidney develops and how the molecular basis of nephrogenesis goes away in congenital kidney disease [10].

According to available data, renal vessels, particularly arteries, are characterized by an extensive range of variability in sources of origin, topography, branching, spatial relationships of branches, and syntopy with other anatomical structures, by number and morphometric characteristics [11]. Due to clinical significance, questions about the anatomy of the renal vessels are constantly attracting the attention of researchers. For different specialists, it is necessary to understand and detect variations, abnormalities, levels, and expressions of them. Anatomical and clinical medical literature describes numerous and diverse variants of the structure of the arterial vascular system concerning the place of discharge, direction, type of branching of vessels, their relationships with surrounding authorities, and blood supply areas [12]. At present, interest in possible variants and anomalies of the vascular system is still considerable

since they may not affect only pathogenesis and clinical manifestations of various diseases but also the choice of treatment methods. In most cases, knowledge of morphological variants of kidney blood supply is significantly helpful in laparoscopic operations and transplantation surgeries where microvascular techniques are employed to reconstruct the renal blood vessels [13]. Variations of the renal arteries have been studied by different authors and published across various population groups [14].

Despite that, the literature is silent regarding morphometric data of renal arteries for cadaveric studies in Latvia, and information about it needs to be included. Therefore, this study aims to detect the variations of the renal arteries, make their and kidneys measurements in our cadaveric samples, and, based on a literature review, correlate the results with those already published.

2. MATERIALS AND METHODS

Under the supervision of an experienced dissector, the routine abdominal retroperitoneum standard anterior dissection was conducted for medical undergraduates at the Department of Morphology. This study was approved by Research Ethics Committee at the Rīga Stradiņš University and a permit was issued in April 2023 (11 April 2023; Nr. 2-PĒK-4/373/2023). The Laboratory of Anatomy of the Institute of Anatomy and Anthropology of Rīga Stradiņš University provided the material. The kidneys of the formalin-fixed five adult cadavers were used for the investigation. Only cadavers with two kidneys were selected for dissection, ensuring the relevant renal anatomy was not distorted. The specimens were placed supine position with their arms lying alongside them.

Perirenal fat and surrounding tissues were removed, and kidneys and the adjacent part of the aorta and arteries were cleared and explored using a Vernier measuring device, roller, and a protractor. For each cadaver, the following parameters were determined and evaluated for each side: the number of renal arteries; the length of the main renal artery; the diameter of the main renal artery at emergence from the aorta; the number of accessory arteries; the presence of early branching; angles between the lateral side of the abdominal aorta and the lower side of the renal artery; kidney length and width. The length of the renal artery was measured from the point of origin to the point of branching as well as from the point of origin to the hilum of the kidney. The diameters of arteries were measured at a distance of 15 mm from their origin in the abdominal aorta. Schematic diagrams were prepared by the authors and visualized all cases of

renal arteries.

Quantitative variables were determined by mean, minimum, and maximum. The analysis included descriptive statistical methods.

Also, this study focused on making out the differences in the variations by comparing them with the previous studies undertaken.

3. RESULTS

The findings of five cadavers' cases concerning the number of renal arteries on both sides, origin, length, diameter, and angle are represented in Table 1 and Table 2.

3.1. Number of renal arteries

In cadaveric cases no. 1-4, one main renal artery (a. renalis) was present on the right side, but in cases no. 1-3 and 5, one main artery was detected on the left side. There was found one main renal artery and one accessory renal artery (a. renalis accessoria) in case no. 5 on the right side and in case no. 4 on the left side.

Table 1. Right renal arteries characteristics in five cadaver cases.

Values of renal arteries	Case no. 1	Case no. 2	Case no. 3	Case no. 4	Case no. 5	
Number	1	1	1	1	1	1
	MRA	MRA	MRA	MRA	MRA	ARA
Origin ¹	L2 (inf)	L1 (inf)	L2 (inf)	L2 (inf)	L1 (inf)	L4 (inf)
Length (mm)	56.0	47.0	21.0	42.0	36.0	65.0
Diameter (mm)	6.5	4.8	7.5	5.6	6.2	3.5
Angle	81°	83°	80°	76°	58°	115°

¹ MRA = main renal artery; ARA = accessory renal artery; L = lumbar vertebra; inf = inferior border.

Table 2. Left renal arteries characteristics in five cadaver cases.

Values of renal arteries	Case no. 1	Case no. 2	Case no. 3	Case no. 4	Case no. 5	
Number	1	1	1	1	1	1
	MRA	MRA	MRA	MRA	ARA	MRA
Origin ¹	L2 (inf)	L1 (med)	L2 (inf)	L2 (inf)	L2 (med)	L1 (inf)
Length (mm)	37.0	28.0	28.0	32.0	68.0	36.0
Diameter (mm)	6.0	4.2	7.8	5.8	1.25	6.2
Angle	71°	110°	107°	74°	74°	58°

¹ MRA = main renal artery; ARA = accessory renal artery; L = lumbar vertebra; inf = inferior border; med = middle.

3.2. Origin of renal arteries

In all our cases, the renal artery starts from the abdominal aorta. There was no case where the renal artery originated from the common iliac, testicular, ovarian, suprarenal artery, or any other source. On the right side, most main arteries originated at the level of the inferior border of L2 and L1. The detected right accessory renal artery started at the level of the inferior border of L4. On the left side, in cases no. 2 and 5, main arteries originated at the level of the middle or inferior border of L1, but in cases no. 1, 3, and 4, these arteries started at the level of the inferior border of L2. The left accessory renal artery began at the level of the middle of L2.

3.3. Length of renal arteries

The length of the right main renal artery fluctuated from 21.0 to 56.0 mm, averaging 40.4 mm, but on the left side, was ranged from 28.0 up to 37.0 mm, averaging 32.2 mm. In case no. 5, the length of accessory renal arteries varied more pronounced (65.0 mm on the right and 68.0 mm on the left) than the length of the main renal arteries (36.0 mm on the right and 32.0 mm on the left).

3.4. Diameter of renal arteries

The diameter of the main right renal artery ranged from 4.8 to 7.5 mm, averaging 6.1 mm, but the diameter of the main left renal artery ranged from 4.2 to 7.8 mm, also averaging 6.0 mm. In the presence of one accessory artery, the diameter of the main renal artery varied from 5.8 to 6.2 mm. In case no. 5, the mean diameter of the presented accessory renal artery was 3.5 mm on the right side, and in case no. 4, it was 1.3 mm on the left side.

3.5. Angle between aorta and renal arteries

The angle between the aorta and the main renal arteries varied from 76° to 83° on the right side, averaging 75.6°, while that angle on the left side was from 58° to 110°, with a mean of 84.0°. The angle between the aorta and right accessory artery was 115° (case no. 5), but the angle between the aorta and left accessory artery was lesser and reached 74° (case no. 4).

3.6. Length and width of the kidneys

Morphometrical measurements of the kidneys are presented in Table 3 and Table 4.

Table 3. Right kidney morphometry.

Values of kidneys	Case no. 1	Case no. 2	Case no. 3	Case no. 4	Case no. 5
Length (cm)	13.0	9.5	10.2	13.0	12.3
Width (cm)	7.6	6.0	5.9	5.4	7.5

Table 4. Left kidney morphometry.

Values of kidneys	Case no. 1	Case no. 2	Case no. 3	Case no. 4	Case no. 5
Length (cm)	15.3	9.1	11.1	11.4	12.2
Width (cm)	7.1	10.7	5.8	6.3	7.7

The length of the kidney varied from 9.5 cm to 13.0 cm with an average value of 11.6 cm on the right side and from 9.1 cm to 15.3 cm with an average value of 11.8 cm on the left side. In cases no. 1 and 4, the length of the right kidney was equal to 13.0 cm. On the left side of all five cases, the values of renal length differed from each other. In cases no. 1 and 3, the left side kidneys were longer than the right kidneys, and the difference was 2.3 cm and 0.9 cm between both sides' length values. In cases no. 2 and 4, the right kidney length values were more prominent than the left side. In these cases, the right kidneys were 0.4 cm and 1.6 cm larger than the kidneys on the left side. In case no. 5, the difference was minimal and only 0.1 cm between the length of the right and left side kidneys.

The values of the renal width varied from 5.4 cm to 7.6 cm with an average value of 6.5 cm on the right side and from 5.8 cm to 10.7 cm with an average value of 7.5 cm on the left side. Compared renal width values between sides, right kidneys were detected wider in cases no. 1 and 3, but left kidneys were wider in cases no. 2, 4, and 5. The renal width differences were 0.5 cm (in case no. 1), 4.7 cm (in case no. 2), and 0.9 cm (in case no. 4). Minimal differences between both side renal widths were in case no. 3 and 5, accordingly 0.1 cm and 0.2 cm.

3.7. Prehilar branching

In case no. 1 (Figure 1), the right renal artery divided into anterior (AD) and posterior (PD) divisions. From the AD straight away after bifurcation started a. segmenti inferioris (ASI). Independently from AD originated a. segmenti superioris (ASS). A. segmenti anterioris superioris (ASAS) and a. segmenti anterioris inferioris (ASAI) started from the common trunk of the AD. PD terminated with a. segmenti posterioris (ASP). The left

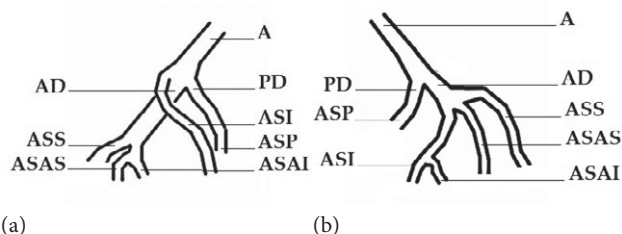


Figure 1. A diagram demonstrating renal artery prehilar branching, case no. 1: (a) a. renalis dextra; (b) a. renalis sinistra. A = a. renalis; AD = anterior division; PD = posterior division; ASS = a. segmenti superioris; ASAS = a. segmenti anterioris superioris; ASAI = a. segmenti anterioris inferioris; ASI = a. segmenti inferioris; ASP = a. segmenti posterioris.

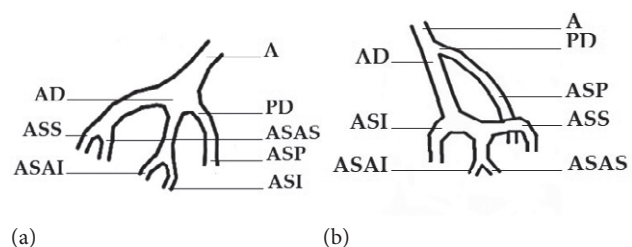


Figure 2. A diagram demonstrating renal artery prehilar branching, case no. 2: (a) a. renalis dextra; (b) a. renalis sinistra. A = a. renalis; AD = anterior division; PD = posterior division; ASS = a. segmenti superioris; ASAS = a. segmenti anterioris superioris; ASAI = a. segmenti anterioris inferioris; ASI = a. segmenti inferioris; ASP = a. segmenti posterioris.

kidney artery was also divided into AD and PD. From one common and short trunk of AD started two branches (ASS and ASAS). ASAI and ASI originated together from another common bifurcated and long trunk of the AD. ASP also was a terminal end of the PD.

In case no. 2 (Figure 2), anterior (AD) and posterior (PD) divisions with their branches started from the trunk of the right kidney artery. At the same level, AD bifurcated again into two other trunks. A. segmenti superioris (ASS) and a. segmenti anterioris superioris (ASAS) together originated from the first common trunk, where a. segmenti anterioris inferioris (ASAI) and a. segmenti inferioris (ASI) started from the second common trunk. The left kidney artery branched into AD and PD. ASS and ASI originated from the bifurcation of AD independently, whereas ASAS and ASAI started from the following common and bifurcated trunk of AD. PD terminated with a. segmenti posterioris (ASP) on both sides of renal arteries.

Case no. 3 (Figure 3) had similar branching of the right and left renal arteries into anterior (AD) and posterior (PD) divisions. A. segmenti anterioris superioris

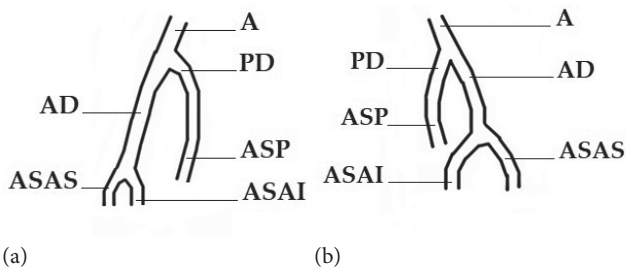


Figure 3. A diagram demonstrating renal artery prehilum branching, case no. 3: (a) a. renalis dextra; (b) a. renalis sinistra. A = a. renalis; AD = anterior division; PD = posterior division; ASAS = a. segmenti anterioris superioris; ASAI = a. segmenti anterioris inferioris; ASP = a. segmenti posterioris.

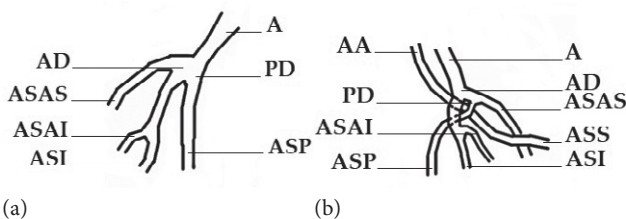


Figure 4. A diagram demonstrating renal artery prehilum branching, case no. 4: (a) a. renalis dextra; (b) a. renalis sinistra. A = a. renalis; AA = a. renalis accessoria; AD = anterior division; PD = posterior division; ASS = a. segmenti superioris; ASAS = a. segmenti anterioris superioris; ASAI = a. segmenti anterioris inferioris; ASI = a. segmenti inferioris; ASP = a. segmenti posterioris.

(ASAS) and a. segmenti anterioris inferioris (ASAI) originated from AD after its bifurcation and on both sides of renal arteries. PD's right and left a. segmenti posterioris (ASP) terminal ends had no branching.

In case 4 (Figure 4), the difference between the right and left kidney arterial systems was detected. On the right side, the anterior (AD) and posterior (PD) divisions, with their branches, started from the trunk of the renal artery. A. segmenti anterioris superioris (ASAS) moved away independently, but a. segmenti anterioris inferioris (ASAI) and a. segmenti inferioris (ASI) originated from another following common and bifurcated trunk. The left renal artery had a more complicated branching, where this kidney was supplied by two arteries: a. renalis (A) sinistra and a. renalis accessoria (AA) sinistra. The second artery moved behind the first artery and terminated as a. segmenti superioris (ASS). The renal artery divided into AD and a short, bifurcated trunk into ASAI and ASI in its following course. PD started shortly after the division place of the renal artery, and it moved away from AD. PD terminated with a. segmenti posterioris (ASP) on both sides of renal arteries.

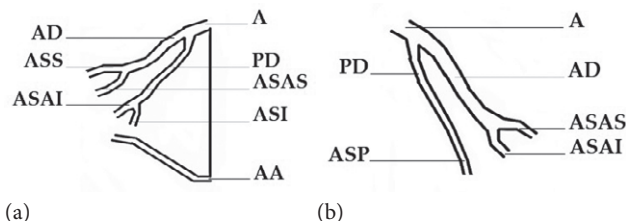


Figure 5. A diagram demonstrating renal artery prehilum branching, case no. 5: (a) a. renalis dextra; (b) a. renalis sinistra. A = a. renalis; AA = a. renalis accessoria; AD = anterior division; PD = posterior division; ASS = a. segmenti superioris; ASAS = a. segmenti anterioris superioris; ASAI = a. segmenti anterioris inferioris; ASI = a. segmenti inferioris; ASP = a. segmenti posterioris.

Case no. 5 was the most interesting occurrence in this study (Figure 5). The right kidney had additional a. renalis accessoria (AA), derivate from embryonic development during metanephros formation in the pelvic region and after ascending to L2-Th12. During this process, there temporary kidney artery that supplied the kidney during its ascending was formed. Commonly this artery was degenerated, but in this case, it was saved. The right renal artery divided into the anterior (AD) and posterior (PD) divisions, bifurcating again into different branches. A. segmenti superioris (ASS) and a. segmenti anterioris superioris (ASAS) started from AD, but PD divided into a. segmenti anterioris inferioris (ASAI) and a. segmenti inferioris (ASI). The left kidney artery divided into AD and PD, where the last one had a lesser diameter than AD. After AD bifurcation, ASAS and ASAI originated, but PD terminated with a. segmenti posterioris (ASP).

4. DISCUSSION

Renal vasculature plays an essential role in several fields of medicine, including introductory study courses like human anatomy, histology, and physiology until clinical study courses in pathology, nephrology, and surgery.

Several anatomic variants of the renal blood supply and their clinical relevance motivate numerous researchers to find a reliable method of visualizing the renal arteries [15]. One of the noninvasive preoperative planning methods for evaluating anatomic variations is multidetector computed tomography (MDCT) angiography [16]. In the case of multiple arteries, it means accurately detecting either incidental kidney pathology or even disease of the artery itself [17]. Kidneys with double arterial supply are involved in a higher percentage of transplant failures than normal kidneys because

double renal arteries can also increase the complexity of renal transplantation [18]. All renal arteries must be anastomosed during this procedure since it appreciates that intrarenal crossegmental anastomoses between arteries are non-existent except for extracapsular and small capsular anastomoses [19]. In the visualization of the relationship between the damaged parenchyma and the architecture of the renal vessels, more advantages are for selective renal angiography [20]. Combining the two investigation methods allows a more complex analysis of morphological parameters, trajectories, and vascular territories of kidneys [21]. Related to this, knowledge of the patterns provides essential data to the radiologists and preoperative information to the surgeons in better planning, the safety of the procedures, and limiting significant complications [22,23]. Nowadays, any info about vascular anomalies is of utmost importance as it influences technical aspects of surgery, results of donor nephrectomy, renal transplant, repair of abdominal aorta aneurysm, urological procedures, and angiographic interventions [24].

The complexity of the topographic and anatomical relationships of the vascular organs of the human retroperitoneal space attracts the attention of researchers. The anatomical configuration of the kidney arteries has a high value in kidney transplantation, nephrology, and different diagnostical manipulations of these fields. Analysis of the literature indicates that the coverage of various aspects of the anatomy and topography of the renal vessels, their variability, and anomalies is still sometimes unambiguous and sometimes contradictory.

The structure of the blood supply is very closely connected in a way to the functional significance of the organ and also depends on the characteristics of its development in embryogenesis. The more complex the organo- and organ histogenesis is in prenatal development, the more its vessels' morphological and topographic features are more pronounced. In the case of abnormal topography or extra artery formation due to adaptation to renal location or due to different embryological aberrations, it may be associated with other clinically significant complications as renal artery thrombosis, stenosis, which can lead to segmental parenchymal necrosis and increased chance of bleeding [25,26]. Mohammed et al. [27] stated that variations in the kidney arterial supply reflect how the vascular supply continually changes during embryonic and early fetal life. Stojadinovic et al. [28] underlined that variations of the main renal artery and vein are common due to several mesonephric arteries during fetal life.

After entering the hilum, each artery divides into five segmental arteries that do not freely anastomose

with each other. The study by Shakeri et al. [29] reports that the apical, upper, middle, and lower segmental arteries usually are from the anterior division of the main renal artery, while the posterior segmental artery originates from the posterior division.

The abdominal part of the aorta is a primary source of kidney supply due to the central and accessory renal arteries. According to the literature, these arteries can be single or multiple. Changes in the number of them are common, ranging from 9% to 76% [30]. In different studies, the branching of the main renal artery varies between 4.3% and 13% [31]. In the current investigation, ten main renal arteries, of which five were on the right side and five on the left side, originating from the aorta, were observed in all cadavers. In the study of 356 kidneys, Abdessater et al. [32] detected 69% a single artery and 31% multiple arteries, including 26% with two arteries and 5% with three or more. Results of other authors showed that the frequency of numerous kidney arteries is about 30% [33,34].

The percentage of frequency of multiple kidney arteries varies from study to study, which can be the reason for complications in its classification and interpretation of results. As reported by Tardo et al. [35], 93.1% of cadavers have one kidney artery, 5.6% have two arteries, and only 1.4% have three kidney arteries. The situation is complicated by the confusion of the terminology that various researchers propose when covering this problem. According to some authors, in the presence of the main arterial trunk and one or more additional arteries, discussing multiple renal arteries, one of them is the main one, and the other (others) - is additional (different) [36]. Other authors consider that it is necessary to distinguish between the concepts of “multiple mains,” “accessory,” and “perforating” arteries of the kidney [37]. Related to VonAchen et al. [38], accessory renal arteries were markedly more prevalent in hypertensive patients compared to normotensive renal donors. The accessory arteries perfuse anatomically equivalent kidney regions and vary in number from two to six. Under multiple arteries, it is proposed to understand the presence of more than two vessels that follow from the aorta to the hilum of the kidney. These kidney arteries can originate from other sources: common iliac, external iliac, celiac, middle suprarenal, right colic, right branch of the hepatic artery, lumbar arteries, etc. In two our study cases, one right and one left accessory renal artery also arose from the aorta.

The renal artery's typical origin is at the L1-L2 intervertebral discs. Kadir et al. [39] observed that in 75% of the general population, the main renal artery arises at the level of the L1-L2 intervertebral discs and in 25% between T12 and L2 intervertebral discs. Özkan et

al. [40] described a single main renal artery as a direct branch of the aorta, originating from the superior edge of L1 and inferior edges of L2 in 98% of individuals. 23% of the right renal arteries and 22% of the left renal arteries appeared between the L1 and L2 intervertebral discs. However, some authors testify that this level is lower and corresponds to the L3 vertebra [41]. In rare cases, on the contrary, a more cranial origin of the renal arteries exists Th12 vertebrae or even supradiaphragmatically. Some authors report that the most typical site of origin of renal arteries from the abdominal aorta is lateral, but less commonly are anterolateral and posterolateral at the level of L1-L2 [42]. In three specimens of this study, the origin of the main renal artery was at the lower border of L2 on both sides. Two right main renal arteries had an origin at the lower border of L1. The left main renal artery in one cadaver started at the lower border of L1. In other cadavers, the left main renal artery originated from the middle level of L1.

The level of origin of the accessory renal arteries from the abdominal part aorta is also variable [43]. It ranges from the lower half of the body of the Th12 vertebra to the lower half of the L3 vertebral body. In this study, the accessory renal artery had a more inferior origin on the right than the left side (lower border of L4 and middle level of L1, accordingly).

Current data showed that the lengths of arteries were not highly different from other studies, but kidney lengths were variable compared to the reported results by El-Reshaid et al. [44]. We found that the mean length of the right main renal arteries was 40.4 mm, and for the left main renal arteries, it was 32.2 mm. The length of the right-sided main renal artery varied from 21.0 to 56.0 mm, whereas the length of the left-sided main renal artery ranged from 28.0 mm to 37.0 mm. The right accessory renal artery length was 65.0 mm, and the left accessory renal artery was 68.0 mm.

The next aspect, important for practical medicine, is a complex of studies of the diameter of the renal artery. Typically, each kidney receives one renal artery with a diameter of about 6-8 mm, but this varies depending on the size of the kidneys [45]. In a study by Bouzouita et al. [46], the renal artery's mean diameter (caliber) was detected as 4.67 mm. The diameter of the right renal artery was 4.83 mm, whereas the left renal artery measured 4.70 mm, but in casts with multiple renal arteries, the mean diameter was 3.40 mm. In this study, results showed that the mean diameter of the right main renal arteries was 6.1 mm but on the left side, for the main renal arteries, it was 6.0 mm. The diameter of the right accessory renal artery was 3.5 mm, and the diameter of the left accessory renal artery was 1.3 mm.

Tarzamni et al. [47] demonstrated that the origination angle of the main renal artery from the aorta did not play a role in the development of the accessory renal artery or its early branching. The authors indicated that the angle ranged from 23° to 110° (mean 57.5°). In current study, the mean angle between the aorta and the main renal arteries was 75.6° on the right side, but on the left, it was 84.0°. Detected 115° angle between the aorta and one right accessory artery was more prominent than the 74° angle in one left accessory artery. In studied case no. 5, on the right side, the angle was the largest, but the diameter of the accessory renal artery was small.

Values of normal renal morphometry are essential for understanding the presence or progression of the disease. The average length usually reaches 12 cm, while the width is approximately 6 cm [48]. Renal size varies and relates to age, gender, height, weight, body mass index, and diseases [49]. Data from this study showed that the mean length of the kidney was 11.6 cm on the right side and 11.8 cm on the left side. In two cadavers, on the right side was seen that the length of the kidney was equal to 13.0 cm. These kidneys were more prolonged in comparison with other right side kidneys. On the left side, one kidney was seen as the longest (15.3 cm), but one kidney was the shortest (9.1 cm), comparing this side to other specimens. As a result, the mean values of the renal width were lesser on the right side than the mean value on the left side (6.5 cm and 7.5 cm, respectively). Compared renal width values between sides, the widest kidney (10.7 cm) was detected in one case on the left side. The narrowest kidney (5.4 cm) was present on the right side. In three cases, the values of the renal widths were almost equal on both sides.

In 2019, Terminologia Anatomica included two branches of the renal artery (anterior, posterior) and five segmental arteries: four from the anterior branch (a. segmenti superioris (ASS), a. segmenti anterioris superioris (ASAS), a. segmenti anterioris inferioris (ASAI), a. segmenti inferioris (ASI)) and one from the posterior one (a. segmenti posterioris (ASP) renis) [50]. In this study, prehilum branching based on the origins of these segmental arteries was analyzed. The segmental branches arose from the main renal artery some distance before it reached the hilum. The number of the prehilum branches varied between two and four. Mostly, the segments were supplied by their arteries, which arose from the anterior and posterior divisions of the main renal artery. These segmental arteries were end arteries. Weld et al. [51] underlined the possibility of the segmental arteries' common origin and introduced the expression "segmental arteries." In all cases, there were observed different

prehilar branching patterns of the renal artery. In some cases, the segmental arteries originated as independent branches, while in other cases, they originated from common trunks with similarities or differences between sides. The prehilary branching of the renal artery has a high level of variation, and it has been discussed previously by several authors [52]. In 1954, the standard classification of kidney blood supply by Graves didn't include all variations, and Shoja systematized them into 8 “cardinal” and 10 “infrequent” groups [53]. Generally, analyzed data of this study can be included in these prehilary branching patterns, except for the combinations of main and accessory renal arteries together.

There were some main limitations of this study. First, the sample size was small, resulting in a low range of variations. Second, these results can be compared only with a few cadaveric studies.

According to the detection of significant clinical significance, the unique direction of research on variant anatomy and topography of arteries aims to study the topography of these vessels concerning the hilum of the kidney and the features of their branching options.

5. CONCLUSION

Based on a small sample analysis, renal arteries vary according to their number, level of origin, length, diameter, angle, and precise relations. All cadavers have one dominant renal artery originating from the abdominal aorta. In the course near the renal hilum, each artery divides into an anterior and a posterior division, which split into segmental arteries supplying the renal segments. Two cadavers have accessory renal arteries from the aorta above or below the main renal artery. They follow it to the renal hilum, the predominant termination point for renal arterial variations. The accessory renal arteries are smaller in diameter compared to the main renal artery. In the measurements of the length, diameter, angle, length, and width of kidneys, there are differences depending on the side of the body (right / left) in the same cadaver and between them.

Results of this study also show that these cases can be systematized and added to renal branching patterns, but some exceptions exist.

Detection of anatomy of the renal arteries may affect pathogenesis, clinical manifestations of various diseases, and the choice of methods of treatment. In Latvia, further studies are recommended to help better understand the detailed anatomy and the architecture of the renal vasculature.

AUTHOR CONTRIBUTIONS:

Conceptualization, D.T.; methodology, D.T., D.K.; software, D.T.; validation, D.T., D.K.; formal analysis, D.T., D.K.; investigation, D.T., D.K.; resources, D.T., D.K.; funding Acquisition, M.P.; writing—original draft preparation, D.T., D.K.; writing—review and editing, D.T., D.K., M.P.; visualization, D.T., D.K., M.P.; supervision, D.T.; D.K. All authors have read and agreed to the published version of the manuscript.

INSTITUTIONAL REVIEW BOARD STATEMENT

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Riga Stradiņš University (number 2-PĒK-4/373/2023, 11 April 2023).

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Early debates on urination in ancient Greek medicine

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Abstract. Although considerable effort has been made by scholars to reconstruct the discovery of renal function in modern times, little attention has been paid to clarifying the early steps of ideas about urine production in Antiquity. In the oldest literature, the site of urine formation remained undetermined. Later, the bladder was considered the central uropoietic place. The first documents advocating the role of the kidneys are attested in the *Hippocratic Corpus*. In the IV century, Aristotle provided a theory of kidney activity. The Hellenistic and Greek-Roman physicians were aware of the fundamental role that the kidneys play in urine production. The kidneys filtered the urine and separated it from the blood. Thus, the excreting activity of the kidneys was postulated in ancient Greek medicine. This historical note describes the initial development of theories on uropoiesis and the early emergence of ideas that will provide a basic conceptual framework in modern medicine.

Keywords: mechanisms of urination, ancient Greek medicine, blood vessels, bladder, kidneys, history of science.

EARLY TIMES: BLOOD VESSELS AND THE BLADDER

In the II century CE, the great physician, surgeon and philosopher Galen of Pergamon noted that in his day even butchers knew that the kidneys were responsible for the production of urine (*On Nat. Fac.*, I.13, K.2.30-31). But in the Greek medical environment of the V century BCE, things were different. We find the first ideas on urine formation in the *Hippocratic Corpus*, a collection of some sixty medical books mainly written in the Ionian Greek dialect (Craik, 2015; Fox, 2020; Jouanna, 1999). The debate concerns both the site of urine production and the mechanism of urine formation. In some text of the *Corpus*, possibly the most ancient texts, the kidneys are neglected and it seems that urine is formed by a sort of blood filtration at unspecified anatomical sites located in the genital parts. An example of this view is found in *Diseases II* (*Diseases II*, 1), which belongs to the oldest layer of the book probably dating to the middle of the V century (Littré, 1839-61). Here the author sets forth a theory of urine formation that postulates the role of blood vessels in the direct transport of phlegmatic material from the head

to genital organs, from where it is excreted by urination. Both the kidneys and the bladder are entirely neglected in this account. The site of urine formation is left completely undetermined. Transported by blood vessels, the phlegm is apparently transferred directly into the urine flowing through the genitals. *Diseases IV* probably dates somewhat later than *Diseases II*, namely to the end of the V century or the beginning of the IV. In *Disease IV (Diseases II, 35)*, a very similar account is reported. The flegm descends from the head through the blood vessels, but here the author states that such humor is sent through the bladder and passes to the outside. The Greek term *diapherō* used in this context implies a movement of fluid across the wall of the bladder. The same mechanism of diuresis is explained in *Regimen in acute diseases (Regimen in acute diseases, 51)*, a treatise dating back to the end of the V century. Here it is reported that the white wine is helpful in acute diseases because “it enters the bladder more easily than the others, and has a diuretic and purgative effect”. Again, the bladder appears as the primary site of urine formation. Only the bladder is mentioned in these passages, not the kidneys. *Ancient medicine* is an important doctrinal text which dates to the end of the V century. In chapter 22, the author includes the bladder among the parts of the body that are hollow. Hence, this structure can expand and contract to attract and release fluids. *Places in Man*, another ancient foundational treatise of the *Hippocratic Corpus*, clearly states in chapter 8 that “the bladder filters the liquid”. The Greek term used here to express this function is *diētheō*, whose meaning is ‘to filter’, ‘to strain through’, ‘to percolate’, and also ‘to purify’. Thus, as the bladder expands and increases in volume, the cavity attracts fluids that seep into the organ and are filtered by its wall. This concept is clearly stated in an illuminating passage from *Diseases of Woman I (Diseases of Woman I, 2)*, a treatise whose content may date back to the middle of the V century. When the matrix is filled with blood, it dilates and presses against the bladder. This in turn ‘attracts the thinnest part of the blood’ contained in the uterus, and the urine becomes red. The effect of attraction is expressed by the verb *eryō*, which means ‘to drag’, ‘to draw’, ‘to pull’, ‘to attract’, ‘to absorb’, implying force or violence. The bladder appears to function like a suction apparatus, a sucker that pulls the fluids that seep through its wall along with it. A further remarkable passage is found in the same treatise (*Diseases of Woman I, 61*), where it is said that the excess fluid of a hydropic woman ‘seeps through (or enter) the bladder’ and is partially excreted by micturition. The verb used to express percolation of the fluid in the bladder is *dierchomai*, which means ‘to go through’, ‘to pass through’,

‘to arrive’. Thus, in some texts of the *Hippocratic Corpus* the place of urine synthesis is either left undetermined or is identified with the bladder. This viewpoint may represent the oldest one. This assumption is agreed to by the *Anonymus Londinensis*, the anonymous author of a medical papyrus probably from the second half of the I century CE, a short compendium of medical ideas which appears to be taken in part from the *Menoneia*, a collection of medical opinions written by Aristotle’s pupil Menon, who asserted that there was a controversy among the ‘ancient scientists’ (*hoi archaioi tōn philosophōn*) (Manetti, 2011; Ricciardetto, 2016). Some indeed maintained that the bad fluid was ‘carried downward and excreted outside by urination’. Others, that the fluid taken in excess was carried ‘to the parts around the region of the bladder’ whence it was converted into a pungent and salty fluid, the urine, which was absorbed by the bladder. It is possible that both positions reflect an older culture rooted in popular belief and Greek folklore that ignored the role of the kidneys in urine formation. In the *Iliad*, the bladder is cited in two passages. By contrast, the kidneys are never mentioned in Homeric poems. In *Iliad XXI.204*, there is only a marginal reference to the ‘fat that lies upon the kidney’ (*dēmos epinephridios*). The redaction of the Homeric poetry is in the VIII century BCE, but material goes back to earlier centuries and the Mycenaean age. This may indicate that the ‘Homeric culture’, as the Egyptian medicine, was unaware of kidney function (Nunn, 1996).

THE KIDNEYS ENTER THE STAGE

Internal Affections is a hippocratic treatise which may be dated to the first decade of the IV century. Here, we find an early indirect allusion to the kidneys as the site of urine production and the clinical picture of kidney stones or nephrolithiasis (*Internal Affections, 14*). In addition to various symptoms, the author mentions the excretion of sandy concretions which, he emphasizes, are formed in the kidneys. Nephrolithiasis originates in the kidneys – the author explains – and should be distinguished from lithiasis of the bladder. The authors of *Nature of Man* and *Aphorisms* write that the finding of small pieces of hair-like, fleshy bodies in the urine is a sign of renal secretion, possibly in connexion with rheumatic fever (*Nature of Man, 14* and *Aphorisms, 4.76*). The Greek verb attested in *Aphorisms 4.76* is *ekkrinō*, whose meaning is ‘to sort out’, ‘to separate’, ‘to expel’, ‘to secrete’. Thus, the kidney is compared to a gland which secretes urine or other constituents. Furthermore, in *Aphorisms* a connexion is made between the excre-

tion of blood in the urine and the breaking of a small vessel in the kidneys (*Aphorisms*, 4.78). This passage is particularly interesting because it relates blood flow with hematuria. *Nature of Man* and *Aphorisms* are two treatises attributed to the school of Cos. The first is generally dated to the years 410-400; the second, though possibly preserving ancient material, was not written before the IV century. *Glands* is a hippocratic text whose date is disputed (Craik, 2009). Some scholars place this short treatise not before the Hellenistic era. According to others, it belongs to an older period, that is, the end of the V century or the early decades of the IV. In *Glands* (*Glands*, 6), the author states that ‘the kidney has glands (*adenes*)’ and suggests that the liquid flowing in is not absorbed by the kidneys but flows through them down to the bladder. This appears to be the first passage in the medical literature where the kidney is equated with a gland. The assimilation of the kidney to a glandular structure exerting a role in collecting moisture may well represent a fundamental seminal principle of renal physiology. Moreover, in the hippocratic *Nature of bones* we find an explicit admission of the part which the kidney exercises in urine formation (*Nature of bones*, 4). It is stated that “what is drunk is attracted to the kidneys through the vessels. Then, the water is filtered as also through the kidneys”. Remarkably, the function of the kidneys is mediated by blood perfusion through renal vasculature. Again, the verb used to express the filtering activity (*diētheō*) is the same one previously attributed to the bladder. However, the kidney is not the only structure capable of producing urine. Indeed, the sentence goes on to assert that fluids are also filtered through the parts into which the kidneys open, namely the ureters. This is where ‘the urine is filtered out and separated from the blood’. The structure of the ureter thus provides both a filtering and a separating function. *Nature of bones* is a hippocratic treatise of difficult dating. It is a compilation of parts containing material from different sources and from different times. The chapter on kidney function shows a marked interest in anatomy and dissection. This does not argue for an early date of composition. Thus, we can tentatively conceive that the concept of kidney involvement in the mechanism of urine production began to circulate in the Greek medical environment towards the end of the V century and coexisted for a long time with the theory of urine production in the bladder. As late as the first half of the I century BCE, Asclepiades of Bithynia, the founder of the Methodist sect, postulated, according to the testimony of Galen, the existence of narrow, invisible, entirely imperceptible passages in the coats of the bladder. The fluid we drink enters the bladder by first dissolving into vapours

and then condensing back into the liquid of urine. According to the theory of Asclepiades and his disciples, still active in the time of Galen in the II century CE, the kidney was created by Nature for no purpose (*On. Nat. Fac.*, I.13, K.2.32). If we now ask the question about the mechanism by which the kidneys are supposed to produce urine according to the Greek medical literature around the turn of the V century, we can conclude that this action is exerted in two ways: i) by filtration (*Nature of Bones*, 4), and ii) by separation and secretion (*Aphorisms*, 4.76).

THE KIDNEY AS A SIEVE-LIKE APPARATUS

We find the first complete and reasonable account of renal physiology in Aristotle (384-322 BCE). According to the Stagirite ‘the kidneys excrete the fluid residue’ (Marandola et al. 1994). The term used to indicate ‘excretion’ is *ekkrisis*. He writes that urine is produced in the kidney by the percolation through the body of the organ of the superfluous fluid, which passes from the blood vessel into the kidney. *Diētheō* is the verb used to indicate ‘percolation’ or ‘filtration’. The filtered fluid then collects into the middle of the viscus where a hollow structure is to be found. This structure is the pelvis. Aristotle concludes that from the hollow part of the kidneys two sturdy channels devoid of blood (the ureters) lead into the bladder, one from each, and the fluid is passed off through them from the kidneys into the bladder. This invaluable aristotelian description contains the main points regarding renal function and urine production: the blood vessel supply, the kidney filtration activity, the collection of urine, and its excretion through ureters and bladder. It appears to be the most precise theory on kidney activity and the anatomy of the urinary system available at the time.

Galen testifies that all the great physicians in Antiquity, including Diocles of Carysus (second half of the IV century BCE), Erasistratus of Ceos (about 330-255/250 BCE) and Praxagoras of Cos (flourished around 300 BCE), believed that the kidney were ‘the organs for the production of urine’ (*On. Nat. Fac.*, I.13, K.2.30). This function is well expressed by Galen’s formula ‘*organa diakritika tōn ourōn*’, which means that the kidneys are the structures responsible for ‘separating out’ the urine. *Diakritikos* comes from the verb *diakrinō*, which means ‘to distinguish and separate one from the other’, ‘to divide’, ‘to part’. We know nothing about the ideas of Diocles and Praxagoras concerning the function of the kidneys. Unfortunately, we are also completely ignorant of the conceptions of Herophilus of Chalcedon (330/320-

260/250 BCE) on this subject. As for the position of the other great Alexandrian, Erasistratus, Galen informs us that he did not comment on the way in which the kidneys function to produce urine, leaving the question (*On Nat. Fac.*, I.17, K.2.67-69). Moreover, Galen explains that some Erasistrateans near the times of Erasistratus held the view that the kidneys functioned like a sieve in that the renal veins conducted the serous fluid, rather than blood, to the kidneys, a view that, as Galen notes, have flourished for a certain period but was then abandoned. This theory was sharply criticized by Galen himself, who thought it absurd. Why, asks the Pergamene, of the innumerable veins which issue from the vena cava, should blood flow into the others, and the serous fluid be diverted into those leading to the kidneys? Despite Galen's criticisms, the Erasistratean assumption that the kidney could function like a sieve apparatus represents a major intellectual achievement. Even today, the glomerular membrane is viewed as a reticular structure capable of selectively passing or retaining different types of molecules. This idea implies a mechanistic view of animal physiology, the very basic principle on which Erasistratus built his natural philosophy. This idea also entails the complex premise of a certain hydrodynamic pressure which must prevail within the blood vessels in order to force the liquid portion out of the blood. One should consider the possibility that this view of kidney function may have been conceived by Erasistratus himself and disseminated among his students. In the I century CE, Rufus of Ephesus wrote a book *On diseases of the kidneys and the bladder*. Rufus was one of the most influential medical writers of Antiquity. He strongly believes that the kidneys are the sites of urine formation, as diseases of these organs, such as inflammation, suppuration, lithiasis, ulcers, sclerosis, and hemorrhages, cause remarkable changes in the quality and quantity of urine. In the chapter on hematuria, Rufus states that "the proper function of the kidneys is to filter the urine from the blood, and to prevent that which is the color of blood, the blood itself, and other thick material from escaping" (Sideras, 1977). The activity of filtering is expressed by the verb *ētheō*, which means 'to sift', 'to strain'. He writes that in hematuria "the kidneys are no longer able to filter the urine, but, being more dilated, they allow some of the blood to pass out of the vessel and other thick material". Here Rufus is very likely referring to the wideness of the pores in the kidney, the presence of which is thus postulated. So, too, for Rufus the kidneys function like sieves. Although Rufus clearly recognizes that urine is produced by the kidneys, the old belief that the bladder is the site of urine formation still persists with him. In describing and discussing the clinical

symptoms of diabetes, a disease which he calls 'urinary diarrhea', i.e. the 'strong flow of urine', and which he regards as a joint disease of the liver, kidney, ureters and bladder, Rufus gives the remarkable proposition that the patient suffers from polydipsia, what he drinks is immediately converted into urine, his body becomes thin and emaciated, and 'wastes away toward the bladder'. The reception of the ancient teachings of Erasistratus and Rufus can be seen in the *Anatomia Mundini* of 1316, in which Mondino de' Liucci (c.1270-1326), one of the leading anatomists in the Middle-Ages, equates the kidney with a kind of sieve, a *colatorium*, colander, or drainer, whose porosity (*porositates*) allows urine but not blood to pass through (Mondino de' Liucci, 1531). Thus, the urine seeps, is distilled, collected, and poured from the kidneys into the bladder. Another eminent physician was Aretaeus of Cappadocia, who flourished in the I century AD. His descriptions of diseases, such as epilepsy, syncope and diabetes are among the classics of their kind. Aretaeus provides us with valuable information about kidney function. He states that "the remarkable action of the kidneys is to separate (*diakrisis*) the urines from the blood and to secrete (*apokrisis*)" (Hude, 1958). By contrast, the function of the bladder is to allow 'expulsion' (*exodos*) of urine. Thus, the different function of these two organs can be readily distinguished. The kidney is like a gland (*adenōdees*), says Aretaeus, in which small, tickling, sieve-like cavities enable the filtration (*diēthēsīn*) of urine. The fluid is then directed into fibrous ducts, the ureters, that connect the kidneys to the bladder. Again, Aretaeus reiterates the concept that the kidneys perform a complex function: they filter (*diētheō*), separate (*diakrinō*) and secrete (*apokrinō*). In 1666, the glandular structure of the kidney was recognized by Marcello Malpighi (1628-1694). He discovered 'a number of very small glands' (*glandularum minimarum*), i.e., the Malpighian corpuscles or glomeruli or renal *pomula*, which 'immediately catch the naked eye', when a black fluid mixed with spirit of wine was injected into the renal artery and then the capsule of the organ was removed (Malpighi, 1666).

THE KIDNEYS AS A SELECTIVE ATTRACTION MACHINE

Galen openly asserted that the quantity of urine excreted daily clearly shows that all the fluid drunk becomes urine, except that which is eliminated with the dejections or which flows off as sweat or insensible perspiration. He provided empirical demonstration that urine is produced by the kidneys and passes through the ure-

ters into the bladder. In this perspective, he performed a series of elegant ligature experiments that would probably inspire William Harvey many years later, in the early decades of the XVII century, in his investigative approach to the problem of blood flowing (Wilkie, 1965; Shank, 1985). In vivisection procedures, Galen secured the ureters with ligatures. The bladder did not fill while the ureters on the side next to the kidneys were quite full and distended and almost in danger of bursting. When the ligatures were removed from the ureters, these ducts abruptly emptied and the bladder filled with urine (*On. Nat. Fac.*, I.13, K.2.36-37). Galen also addresses the question on how the kidneys would perform their function of separating urine. He argues that one mechanism could be the driving force of the venous blood, the other the attractive faculty of the kidney itself. Galen's line of thought is logical, consequential, and strongly influenced by the basic principles of his general physiology. He approaches the truth, but fails to grasp it. He argues that if the veins were to force the blood into the kidneys, they would squeeze out not only the urine, but all the blood they contain (*On. Nat. Fac.*, I.15, K.2.57). If the kidneys acted like a sieve, letting through the thinner serous part and retaining the thicker portion of the blood, then all the blood contained in the vena cava would have to pass to them to be filtered. But Galen does not know the circular motion of the blood in the sense formulated by Harvey. According to his physiological theoretical principles, the venous blood is produced by the liver and is slowly carried to the periphery by the contraction of the veins. It reaches all organs and tissues where it is assimilated and consumed. Thus, only a small portion of the total volume of blood would percolate through the kidneys. As much as can be contained in the veins leading to the kidneys. So only that portion is purified. If the kidneys were to function like a sieve, the thin serous part of the blood would flow through the organs, while the thick bloody part remaining in the renal veins would obstruct the blood flowing in from behind. The blood must therefore first run back into the vena cava to empty the veins leading to the kidneys, otherwise there will be no passage left for further blood (*On. Nat. Fac.*, I.16, K.2.65). Such a situation implies a number of complex hemodynamic consequences that are difficult to deal with in a non-Harveyan pattern of blood movement. In a sieve-like perspective, Galen equates the process of urine formation with the process of cheese production (*On. Nat. Fac.*, I.15, K.2.58). For even this, though is thrown into the basket strainers, not all seeps through. The part that is too fine in proportion to the width of the meshes flows downward. The remaining thick part, which is destined to become cheese, cannot

get down, because the pores of the strainers will not let it pass. According to Galen's conception, this is the part that obstructs the lumen of the renal veins. Apart from this disadvantage, the kidneys do not have a favourable position to function like a sieve, as they are not situated below the vena cava, but on either side of it. This means that gravity would exert little force on the blood flow directed to these organs. It is therefore impossible for the kidneys to function like sieves. Now, if the movement of urine does not depend on the tendency of a vacuum to be replenished – a general mechanistic hydrodynamic principle advocated by Erasistratus as a general force for the motions of fluids, which was severely criticised by Galen who favoured a vitalistic causation as the attraction of the simile by the simile – then the remaining explanation – as Galen admits – is that the kidneys actually exert a traction force, i.e., a selective movement of fluid. The kidneys possess a specific faculty which draws to themselves the particular quality existing in the urine, as the lodestone attracts the iron. Therefore – Galen concludes – it is impossible to give any other reason for the secretion of urine than the principle of attraction (*On. Nat. Fac.*, II.2, K.2.77-78).

CONCLUSIONS

The early debate about the site of urine production and about the functional model of the kidneys is rich in interesting perspectives. Ancient Greek physicians assumed that urine was formed in the kidney by a process of separation from the blood. Some eminent medical doctors took a mechanistic view and equated the kidneys with sieve-like devices. Moreover, the organ seemed to have an intrinsic secretory capacity. This appears to be a fairly modern view of kidney function. That the hippocratic author of *Glands* and Aretaeus of Cappadocia equate the kidney with a gland seems a fundamental step in understanding the relationship between structure and function of the organ. It is likely that the small, sieve-like cavities mentioned by Aretaeus are the minor calices surrounding the renal papillae. It is noteworthy that, as early as 1521 the Renaissance surgeon and anatomist Jacopo Berengario da Carpi (c.1470-1530) equated the substance of the inner part of the kidney with several female nipples (renal *papillae*), thus equating the kidney with a complex glandular structure that secretes urine in a large cavity situated in the centre of the organ (Berengario da Carpi, 1521). In his seminal 1842 paper, Bowman (1816-1892) himself equates the secretory tubules of the kidney with those of 'all other glands' and refers to 'the nipple-shaped extremi-

ties of the [medullary] cones' to denote the renal papillae (Bowmann, 1842). Given the remarkable structure of the Malpighian bodies and their unique connection with the tubes, Bowmann ventures to speculate that - the tubes and their plexus of capillaries were probably [...] the parts concerned in the secretion of that portion of the urine to which its characteristic properties are due (the urea, lithic acid, &c.), the Malpighian bodies might be an apparatus destined to separate from the blood the watery portion - (Bowmann, 1842). Again, secretion and separation appear to be key concepts that come from ancient Greek science. We must wait for the work of Carl Ludwig (1816-1895) to come up with a radically new concept of kidney function. He was famous for his explanation of glomerular filtration in terms of physical cardiovascular hemodynamic forces, but beyond filtration, separation, and secretion, Ludwig introduced the idea of reabsorption of most of the aqueous portion of urine and other substances dissolved in it, a principle unknown to Greek teaching (Ludwig, 1842).

Nevertheless, Galen's legacy was disappointing. Despite his sophisticated experimental approach and fine theoretical reasoning, the Pergamene's notion of a specific faculty of attraction by the kidneys remains nebulous and physically indeterminate. Unfortunately, Galen's doctrine overshadowed previous contributions and the subsequent history of renal physiology will be a progressive emancipation from the attraction principle and the search for a mechanistic explanation of kidney function (Mc Vaugh, 2012). A remarkable point in ancient Greek medicine was the constant linkage between kidney action and blood perfusion. Urine derived either from blood filtration or a selective attraction from the blood. It is perhaps not coincidence that one of the first medical texts in the Western medieval world, the *Anatomia porci ex Cophonis libro* - a document from the XI-XII century belonging to the Salernitan school of medicine - mentions the tiny blood vessels (*capillares venae*) emanating from the renal vein, so thin that they cannot be traced with the naked eye, through which the urine is conducted to the kidney (de Renzi, 1853). We conclude with the words of Malpighi: - For a long time - he wrote in his introduction to *De renibus* - the kidneys have been the subject of varying opinions, some even having regarded them as superfluous and unnecessary, a thought which is certainly not a tribute to Nature. More recently, however, because of their wonderful structure, and because of the very necessary function attributed to them, they have attained a place among important parts of the body - (Malpighi, 1666).

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A linguistic clarification for four key anatomical terms

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Abstract. This brief note aims to offer some historical and methodological clarification on four key anatomical words (anatomy, dissection, autopsy and prosection) which are often used incorrectly by students and members of the public when referring to human anatomy. The origin, meaning and – for the most important ones – correct pronunciation of the words is given as well as recommendations on how to use them correctly.

Keywords: anatomy, education, history, teaching, review.

INTRODUCTION AND AIM

Human anatomy represents the angular stone on which the edifice of biomedical knowledge is erected. Despite various historical attempts at downsizing its importance, above all its practical component represented by human cadaveric dissection, the discipline is still considered a solid and indispensable step in biology, pharmacy, and medicine students worldwide [1].

A great confusion, nevertheless, appears to exist in the exact use of terms connected with this discipline, both at the students' level, in the general public and in the press.

This realization derives from the authors' personal experience dealing with teaching, examining, and popularizing aspects of the anatomical discipline, or closely related fields such as biological anthropology, bioarchaeology, palaeopathology, etc. at the university level. For this reason, the goal of this brief note is to offer a summary of the origin and exact meaning and preferred uses of the following nouns: *anatomy*; *dissection*; *autopsy*; *prosection*. Before delving into the specific aspects of these words, in Fig. 1 a historical overview is offered of their use approximately in the last five centuries (AD 1500–2019) using the

Google Books Ngram Viewer website, from which, besides the predominance of the word anatomy (reasonably used also in other non-medical contexts) the word *dissection* has become more commonly used than *autopsy* from the second half of the 20th century.

MATERIALS AND METHODS

This concise review adopts a historical approach and explores the etymology, development and use of the words *anatomy*; *dissection*; *autopsy*; *prosection*. Finally, for each term, it offers paedagogical suggestions on when it is best to adopt such words and what wrong used should be avoided by students.

ETYMOLOGY AND CORRECT USE OF THE SELECTED WORDS

Anatomy

It comes from the ancient Greek noun ἀνατομή originating in turn from the verb ἀνατέμνω, literally “I cut up”, composed of ἀνά (“up”) and τέμνω (“I cut”) [2]. In Latin it was ultimately translated as *anatomia* with the stress being laid upon the antepenult syllable, thus being pronounced as /a.na'to.mi.a/, whereas in Italian it became *anatomia*, /a.na.to'mi.a/ (stress on the penult syllable), in English *anatomy* /ə'næt.ə.mi/ still on the antepenult (the word consisting of four syllables in that language instead of five as in Latin or Italian), in French *anatomie*, in German *Anatomie*, with both languages stressing the last syllable instead. The Latinate word *anatomy* now made so popular in the English-speaking-world by Henry Gray's *Anatomy* textbook [3] appears to have entered the English language through its Old French counterpart *anatomie* during the Middle Ages. During the late 14th century AD anatomy primarily meant the “study or knowledge of the structure and function of the human body”, which, as it was understood in those days, could only be attained through dissection. It can be well understood how it represented the discipline, while around the beginning of the 15th century it also started to indicate the “anatomical structure”, that is the very object of the scientific enquiry represented by the word [4].

Subsequently, in Shakespeare's day the word anatomy also counted as a synonym for other related words such as *dissection* (see the above reasons), *mummy* (originally meaning the substance covering embalmed bodies, then such preserved corpses in their entirety), *skeleton* (only a part of the whole human anatomical structure). From the 17th century on it once again indicated primarily the

study or science of the structure of bodies [4]. Both English and Italian versions of the word were often spelt as *natomy* or *notomia* as a result of a linguistic phenomenon known as apheresis (in English the initial ‘an’ also being mistaken for the indeterminate article). Of note, Mondino de' Liuzzi (1275-1326) celebrated masterpiece featured another variant of it, *Anothomia* [5].

It can thus be concluded that the word *anatomy* both indicates the scientific discipline and its subject. Biomedical students are, nonetheless, advised to think of it simply as an abbreviation of *human anatomy*, in that another, much broader branch of this discipline studies not only the bodies of anatomically modern *Homo sapiens*, yet also the remaining members of the animal kingdom and the evolutionary processes at the basis of modernly observed morphologies, thus being referred to as *comparative anatomy*. Students should also recall how their study of human anatomy can be further divided into *macroscopic* and *microscopic* human anatomy and how the former can be studied both *topographically* or *systematically*, depending if their focus be on all the anatomical structures present in a certain bodily district or, on the contrary, on all the structures forming a system throughout the human body.

Dissection

It comes from the Mediaeval Latin word *dissectio*, originating in turn from the union of the praefix *dis-* indicating a separation and the verb *secare*, “to cut”, hence “to cut in pieces” [6]. As it can be immediately seen, this word is very close to aforesaid verb ἀνατέμνω, from which the very word *anatomy* was shown to stem. Nevertheless, it appears to have made its appearance much later than the word anatomy, meaning the scientific opening of the human body – or of animal bodies – for an anatomical study or, more generally, in relation to medicine and its branches. In the latter sense, it can be related to pathologic anatomy and forensic medicine. It reached the English language in the late 16th century AD deriving from the French word *dissection* or possibly directly from the Latin original. From the mid-17th century on, it also developed a more abstract meaning and can thus also be related to the critical examination of things. From *dissection* derives the word *dissector*, that is the person, a scientist, an instructor, or a student, performing the act of dissecting a body [7].

Students of anatomy are advised to refer to *anatomical dissection* when they play an active part in the process, that is when they themselves, under the guidance of experienced teachers and tutors, *dissect* a cadaver in order to perfect their knowledge of its inner structures.

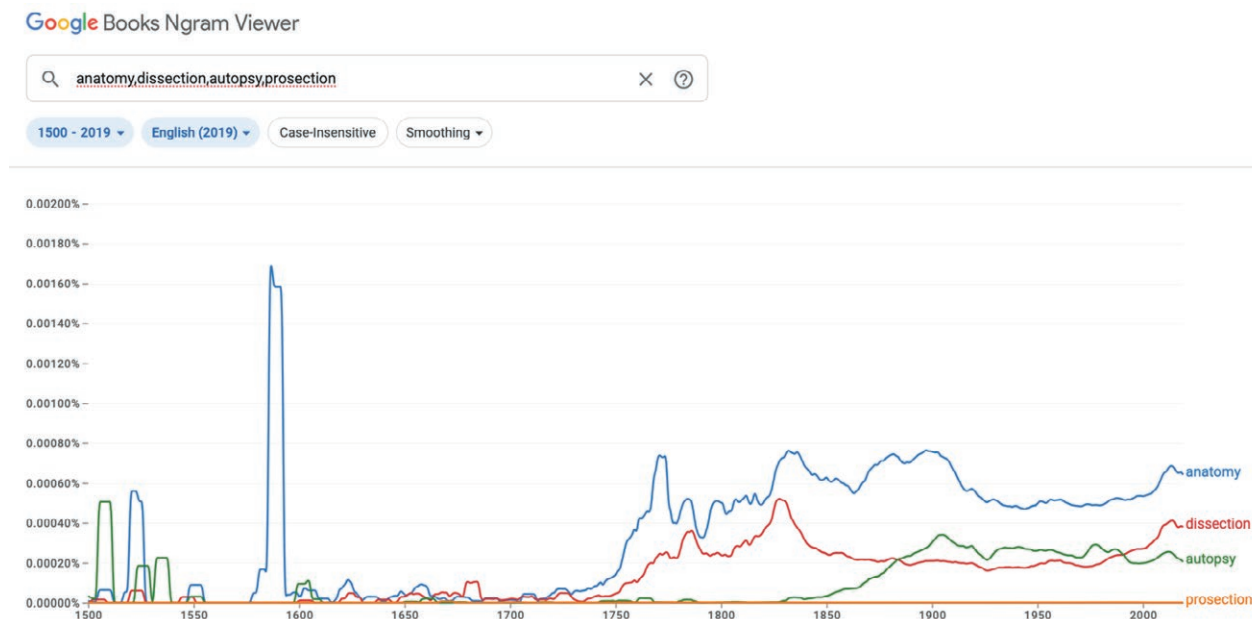


Figure 1. Historical use of the four discussed words from 1500 to 2019, based on books published in the English language. Image generated with *Google Books Ngram Viewer* (online at: <https://books.google.com/ngrams/>).

Dissection should not be confused with prosection, which will be discussed later.

Autopsy

This word, in English (/ˈɔːtɒpsiː/) as well as in other European languages, derives from the neo-Latin word *autopsia* (stress on the penult syllable, /awˈto.psi.a/), which in turns stems from the Greek αὐτοψία, literally meaning “to act of seeing with one’s own eyes”, originating from the union of the words αὐτός (“self”) and ὄψις (“sight”) [8, 9]. Herodotus of Halicarnassus’s (484-430/420 BC) method of inspecting and annotating foreign customs and physical traits is considered an early form of *autopsia* applied to ethnographical matters [10].

Originally, it meant the mere act of seeing anything (i.e. not necessarily a cadaver) with one’s one eyes. When referring to medicine it could meaning the examination of a patient as opposed to the anamnestic collections of information; on the contrary, when referring to a corpse, it did not necessarily include the act of “sectioning a body”. Expressions like *autopsia cadaverica* would emerge only much later (ca. 18th century AD) and could be substituted by other expressions such as *postmortem examination* or *necropsy/necrotomy* [11].

Students of anatomy should know that autopsy does represent a major aspect of the study of the human body in that its structures should not only been passively

memorized but actively observed by them with an investigative attitude, in order to learn them properly. Nonetheless, they should be aware that an autopsy does not always represent a physical dissection of cadavers nor is it limited to forensic aspects.

Prosection

It derives from the Latin *prosectio* (*pro-* “before” + *sectio* “a cutting”). Its earliest known use in English dates back to the 1890s [12]. It refers to the dissection of a cadaver for teaching purposes by an experienced anatomist so that students may observe and touch structures of the human body. They may both observe the anatomist while dissecting a cadaver and examine his preparations later. This represents a valid complement to what can otherwise be learnt from books or theoretical classes [13].

It should, however, be underlined that in such a practice, the students’ role is much more passive than in the actual dissections as seen above. For this reason, anatomy students should not refer to prosection-based curricular activities as dissection-based studies.

CONCLUSIONS

The above-described words have been related to their etymology and use throughout history, highlight-

ing what potential errors students can make when referring to them inappropriately. This is not merely a linguistic aspect – yet still very relevant in educated biomedical students – but also something that can have an impact on their understanding of their curricular steps and play a role in their setting goals as learners and determine their expectations.

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Persistent primitive hypoglossal artery: a case study with a dissertation on its embryopathological rationale

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Abstract. Persistent Primitive Hypoglossal Artery (PPHA) is a developmental anomaly of the brain superficial arterial circulation and is classified as a condition of carotid-vertebrobasilar anastomosis persistence caused by lack of reabsorption of the vascular network running on the hindbrain surface between the 4th and 5th embryonic week. It has an incidence between 0.03 and 0.9%, it is the second most frequent seen persistence of carotid-vertebrobasilar anastomoses after the trigeminal artery (TA), representing 85% of all persistent vestigial arteries (0.1–0.6%). Here a case of Persistent Primitive Hypoglossal Artery (PPHA) is reported being detailed in its morphological and clinical aspects. The patient, a 55-year-old female patient with high cardiovascular risk without specific symptoms presents at radiological morphological examination with an anomalous bifurcation of the ICA which gives rise to the ICA itself, which ascends without collateral branches up to the carotid foramen in the cranial base, and to an accessory artery, which enters the hypoglossal canal on the contour of the great occipital foramen, as a PPHA. A comprehensive embryologic analysis of this anatomical variant is offered and clinical awareness on it raised in view of a more informed and effective realization of it in daily clinical practice.

Keywords: anatomical variant, angiography, congenital, cardiovascular, persistent primitive hypoglossal artery.

INTRODUCTION AND AIM

Persistent Primitive Hypoglossal Artery (PPHA) is a condition of carotid-vertebrobasilar anastomosis persistence due to lack of reabsorption of the vascular network running on the hindbrain surface between the 4th and 5th

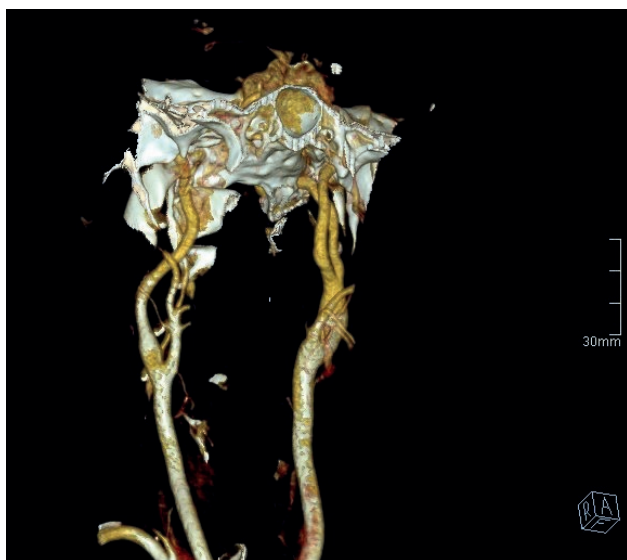
embryonic week; it is included among the developmental anomalies of the brain superficial arterial circulation, which in turn are frequently associated with anomalies in the development of the internal carotid arteries (ICAs). With an angiographic incidence of 0.027 to 0.26% (Zhang et al. 2021), having also been reported up to 0.9% (See et al. 2017), and with a greater frequency in females and a predilection for the left side (Srinivas et al. 2016), it mostly represents an incidental finding detected during radiology carried out for other reasons, as it is associated with a limited symptomatology and presents few significant signs. First described during an anatomical dissection in 1889 (Batujeff 1889), with its first angiographic description dating back to 1961 (Begg 1961), PPHA may occur in association with aneurysms (Nakamura et al. 2000) and its well-known association with the ipsilateral vertebral artery agenesis (VA) seems

to play an ischemic role in the event of inflow reduction in ICA, which alone supplies vascularisation on its own side (Zhang et al. 2016).

Here we report a case of PPHA, which we detail in its morphological and clinical aspects. This single case study will then prompt a discussion on the embryologic rationale of this anatomical variant.

CASE REPORT

A 55-year-old female patient referred to our Cardiology Outpatient Service with a high cardiovascular risk (i.e. smoking, high cholesterol levels) without specific symptoms: since atherosclerosis, as is currently known, is multi-district disease, there is a tendency shared between radiologists and cardiologists to perform a single exam to study both the coronaries and epiaortic vessels, thus benefiting from a single administration of contrast medium. In our specific case, the extension of the study up to the supra-aortic vessels incidentally led to an angio-CT diagnosis of PPHA. The multi-slice CardioSync CT Scan (Siemens Somatom Volume Zoom) for the study of coronary arteries and epiaortic vessels after iodine non-ionic contrast medium administration was used: the volume rendering reconstruction (Fig. 1) of the epiaortic vessels shows an anomalous bifurcation of the ICA, which gives rise to the ICA itself, which ascends without collateral branches up to the carotid foramen in the cranial base, and to an accessory artery, which enters the hypoglossal canal on the contour of the great occipital foramen, as a PPHA. The anomalous ICA bifurcation was confirmed by MIP (maximum intensity projection) reconstruction (Fig. 2), while Multiplanar Reformation (MPR) describes the supra-aortic trunks' courses (Fig. 3).



Figures 1. Volume rendering reconstruction of the epiaortic vessels with evidence of an anomalous bifurcation of the ICA (top and bottom images).

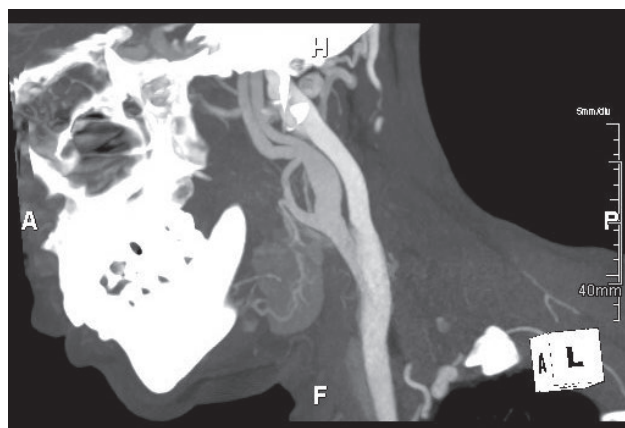


Figure 2. MIP (maximum intensity projection) reconstruction confirming an anomalous ICA bifurcation.

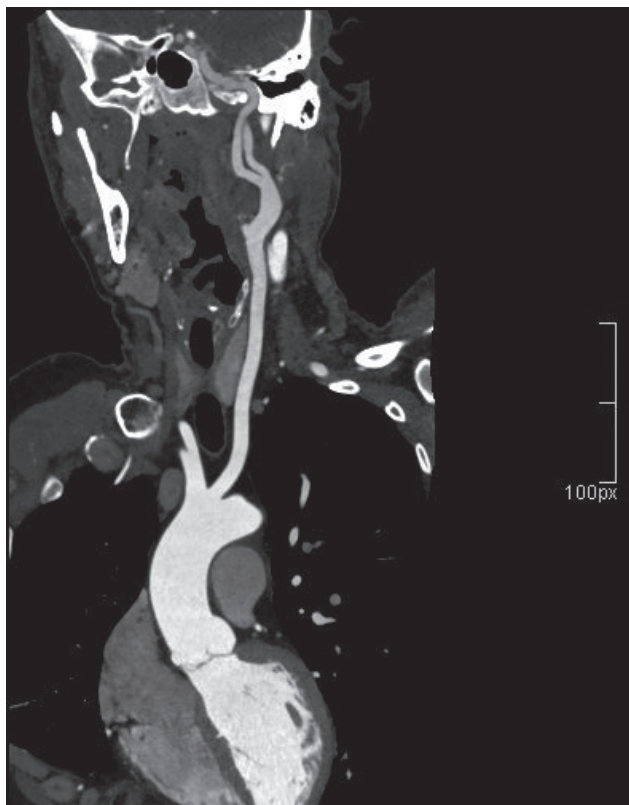


Figure 3. Multiplanar Reformation (MPR) describing the courses of the supra-aortic trunks.

DISCUSSION

a. Embryology

The heart begins to form in the second week of embryonic development (Fig. 4) by the migration to the edges of the trilaminar embryo of pre-cardiac mesodermal cells, which differentiate into cardiomyocytes; by the end of the second week the neural tissue rapid growth causes the flat embryo to fold and tubularise, hence causing the heart to acquire the inverted-Y shape and then (week IV) the S-shaped loop, which will form the cardiac cavities of later life (Buijtendijk et al. 2020). At the beginning located in a cephalic position, the heart then descends into the thorax where its connection with the paired dorsal aorta undergoes changes which will give rise to the adult aortic configuration, via the production and remodeling of six pairs of arteries of the branchial arches. The artery of the first branchial arch first forms the primitive mandibular artery which later becomes the Vidian artery, the dorsal portion of the II branchial arch artery becomes Internal Carotid Artery (ICA) passing through the stages of hyoid and stape-

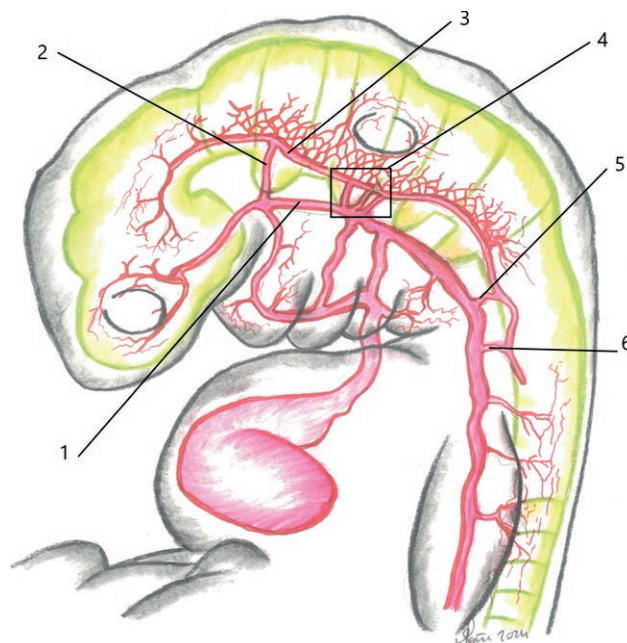


Figure 4. 1. dorsal aorta; 2. trigeminal artery; 3. longitudinal neural artery; 4. otic branches; 5. primitive hypoglossal artery; 6. proatlantal intersegmental artery.

dial, while the ventral portion becomes first the ventral pharyngeal artery and then the External Carotid Artery (ECA). The carotid-tympanic artery is the adult remnant of the II branchial arch artery: the artery of the third branchial arch merges with the distal portion of the double dorsal paired aorta to form the proximal portions of the ICAs, while the artery of the IV branchial arch forms the aortic arch on the left side and the subclavian arch on the right side. The arteries of the sixth branchial arch contribute to the formation of the two primitive pulmonary arteries with their proximate portion, while there is no scientific agreement on the role of the artery of the fifth branchial arch (Klostranee & Krings 2022).

b. Vascular anomalies

The most common vascular anomalies of the vessels of the neck (Fig. 5) include the common origin of the brachiocephalic trunk and left Common Carotid Artery (CCA), the aberrant right subclavian artery, also called *arteria lusoria*, the ICA aplasia or hypoplasia; ICA is embryologically divided into 7 segments (I - cervical, II - ascending petrosus, III - horizontal petrosus, IV - ascending cavernous, V - horizontal cavernous, VI - clinoid and VII - terminal): ICA hypoplasia is frequently seen close to the bifurcation (segment I) (Kathuria et

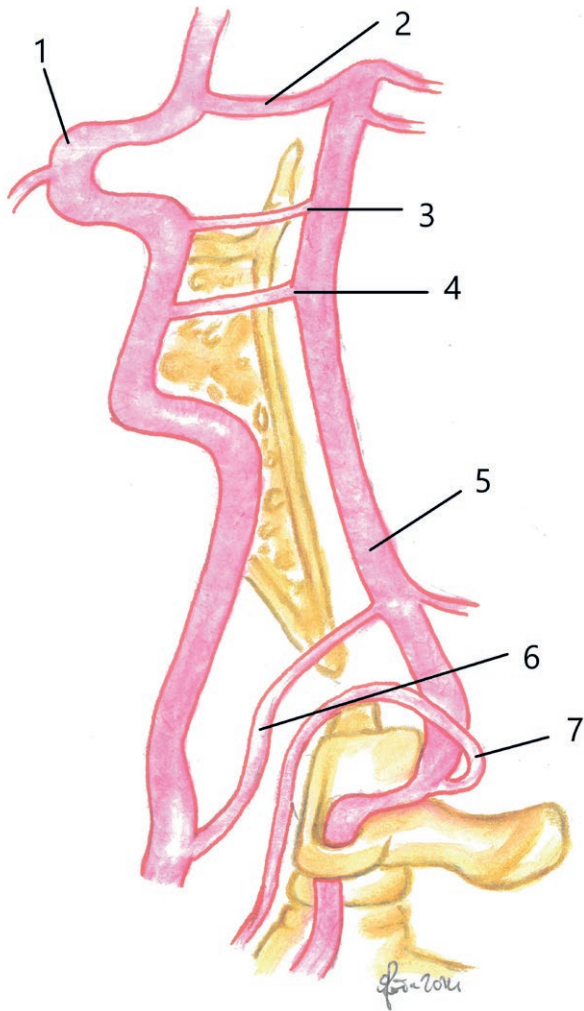


Figure 5. 1. internal carotid artery; 2. posterior communicating artery; 3. trigeminal artery; 4. otic artery; 5. vertebro-basilar trunk; 6. hypoglossal artery; 7. proatlantal artery.

al. 2011), while the aplasia is observed at carotid foramen (segment II, with canal of reduced caliber or even absent) (Given et al. 2001). Two other known anomalies are the aberrant ICA (more common in female), and the persistent stapedial artery (in 3% associated with the absence of the spinous foramen). As regard to the superficial cerebral arteries we recognize 7 chronological and morphological stages of development: stages I and II are observed in the 4th week (development of the vertebro-basilar trunk - VBT - and the posterior communicating artery - PCA), stages III and IV up to the 35th day (formation of basal nuclei vessels, of the ophthalmic arteries, the choroid plexus and the completion of the circle of Willis) and stages V, VI and VII, between 40 and 52 days (vascularization of the remaining superficial cerebral and cerebellar territories) (Klostranee & Krings

2022). In stage I (28-29 days) the ICA bifurcates into an olfactory cranial branch that will become the anterior cerebral artery (ACA) and in a caudal branch that will give rise to the PCA: 4 anastomotic bridges exist between the two ICAs and two parallel neural arteries running on the hindbrain surface. This network is basically formed by transient anastomoses between ICAs and VBT and is represented by the trigeminal artery (TA), the hypoglossal artery (HA), by an otic branch (OB) and a distal proatlantal artery (PAA) (Lie 1968). During stage IV (5-6 mm length) the PCA is completed and the OB, followed by the HA, TA and the distal PAA regress (Coulier 2018). In stage VII the intersegmental PAA continues to vascularize the hindbrain until the complete development of the vertebral arteries (VAs) (32 days, 7-12 mm), which are made up of transverse anastomoses between adjacent cervical intersegmental arteries: later they become sub-occipital intersegmental arteries to move towards the intersegmental artery of C6, to form the origin of the adult vertebral and subclavian arteries.

c. PPHA

The PPHA has an incidence between 0.03 and 0.9% (Kings et al. 2015) and is the second most frequent seen persistence of carotid-vertebrobasilar anastomoses after the TA, representing 85% of all persistent vestigial arteries (0.1 - 0.6%); Persistent TA has been described to cross the sella turcica in 50% of the cases observed, forming a bridge between the ICA, the PCA and the middle third of the VBT: persistent intersegmental PAA is rarer, with fewer than 50 cases described (Tsukamoto et al., 1981) and has a horizontal sub-occipital course that overlaps with that of the VAs, except that there is no transit through the transversal foramina of the vertebrae from C6 to C1 (Anderson & Sonheimer 1976). A persistent OB that establishes an angiographically visible anastomosis with the ICA is largely still debated (Lasjanias et al. 2001). The HA usually rises from the cervical portion of the ICA (C1-C2) and enters the posterior cranial fossa joined with the hypoglossal nerve: A didactic description is provided by the so-called Lie criteria (Lie 1968) which identify the HA originating 1) from the ICA at C1-C3 level as a large branch, 2) passing through the hypoglossal canal after a twisted course, 3) anastomoses with the VBT and 4) it is associated with the radiological absence of the PCA. The VBT appears vascularised beyond the anastomosis with the PPHA and often the VAs are hypoplastic (Elhammady et al. 2007); Brismar (Brismar 1976) added two more criteria: 5) the PPHA can rise from the ICA as an extra-cranial branch 6) and it passes through the condyloid foramen before joining

the distal part of the VBT. Exception to these criteria is represented by the described connection with the inferior posterior cerebellar artery without anastomosis with the VBT (Uchino & Suzuki 2018). Originating more frequently by the ICA (Type I) (Coulier 2018), the PPHA can also have a rare origin from ECA (Type II), in which case an anastomosis with the VA through the hypoglossal canal (Meguro et al. 2007) and one between the ECA and VBT have been observed; more frequent in females and on the left side (Srinivas et al. 2016), it represents an incidental diagnostic finding due to its asymptomatic nature, although exist aneurysms at the PPHA and VBT junction level (26%) (Huynh-Le et al. 2004), and neuralgia, glossopharyngeal palsy and malformations of the craniocervical junction are reported. Abnormal bifurcation of the ICA due to the PPHA may increase the risk of carotid bulb atherosclerosis (Vlychou et al. 2003), while the absence or hypoplasia of the Vas and the PCAs oblige the ICA of the affected side to supply the brainstem, cerebellum and ipsilateral hemisphere alone, exposing to ischemic risk in case of reduction of carotid inflow (De Caro et al. 1995); brain aneurysms associated with PPHA (Nakamura et al. 2000), ICA (Fantini et al. 1994; McCartney et al. 1989) and ECA (Type II) (Welten et al. 1988) atherosclerosis involving the root of the PPHA, PPHA aneurysm within the hypoglossal canal associated with subarachnoid hemorrhage (Kimball et al. 2015), as well as stenosis Doppler signals without angiographic confirmation associated with PPHA (suggesting that this condition may increase arterial flows by simulating carotid stenosis) have been described (Widmann & Sumpio 1992). For this reason, due to a larger-than-normal hemispheric perfusion provided by the ICA, some authors have also suggested routine electroencephalographic monitoring during endoarterectomy (McCartney et al. 1989).

CONCLUSION

The present study and annexed commentary have highlighted the embryonic origin of the anatomical variant represented by the PPHA. It should be stressed that an enhanced knowledge of anatomical variants can allow better diagnoses and therapies by clinicians in their daily practice.

PATIENT CONSENT

The patient signed her written informed consent before the performance of the radiological exams.

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Special issue on teaching in Anatomy

Thinking anatomical science education in the future, beyond the limits

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The study of anatomy holds a pivotal role in the early stages of our country's medicine course degrees. The exploration of standard human body structure is now intricately linked to the study of microscopic anatomy, embryology, and molecular interactions. Anatomy serves as a bridge to physiology, pathology, and a multitude of clinical disciplines, applying knowledge of both normal and abnormal structures.

Considering the continuous and unceasing evolution affecting medical course degrees, nowadays increasingly “problem-based” and where anatomy curricula must necessarily have a more integrated approach, the anatomy teaching must require increasing attention both to curricular parts that need new forms of integration and to the study of new teaching methodologies that, together with what is classical must always be present, must be able to be cutting-edge, integrating with the latest experimental technologies proper to the diagnostic and clinical sciences.

Teaching methodologies also need to be tested, much more today than in the past, to show their validity in each student's educational process. Based on current trends and research findings, the future of anatomical science education is undergoing significant evolution.

Anatomical education is evolving in tandem with the changing landscape of medical education. It integrates anatomical science with clinical implications, such as in minimally invasive surgery, to enrich students' comprehension and preparedness for future medical practice (McCumber et al., 2022). The international development of core syllabuses for anatomical sciences signifies a global commitment to standardizing anatomical education (Moxham et al., 2014). As the field advances, there is an increasing demand for enhanced support for anatomical educators. This collective effort is crucial in upholding the quality of anatomy training in medical and health sciences institutions (Wilson et al., 2020). Integrating new educational technologies, adapting teaching styles, and revising anatomy courses are critical drivers of the evolution of anatomical science education (Pawlina & Drake, 2010).

Cadaveric dissection has been a cornerstone of anatomical education for centuries, providing students with a hands-on experience to observe and understand the complexities of human anatomy. This classical method of learning anatomy through dissection allows students to appreciate the vari-

ability of anatomical structures and develop a comprehensive understanding of the human body. By dissecting cadavers, medical students learn to accept anatomical details as they appear in the human body, fostering a holistic perspective on anatomy (Ghosh, 2016). The dissecting room remains a cornerstone of anatomical science education, offering students a unique and invaluable learning environment. Through cadaveric dissection, students acquire essential anatomical knowledge and skills and develop professionalism, empathy, and respect for the human body. The dissecting room remains a vital space where future healthcare professionals establish the foundation for their medical careers through immersive and experiential learning.

Today, digital technologies have significantly impacted anatomical science education by revolutionizing teaching methods and enhancing students' learning experiences. Integrating digital resources, such as virtual dissection tables, anatomical software applications, and three-dimensional models, has transformed anatomy education (Harmon et al., 2021). These technologies have enabled educators to create interactive and engaging learning environments that cater to diverse learning styles and preferences, ultimately improving students' understanding and retention of anatomical concepts (Xiao & Adnan, 2022). By incorporating multimodal digital resources, educators can enhance contextual learning, promote active engagement, and provide students with a more comprehensive understanding of anatomical structures (Xiao, 2023). Since the COVID-19 pandemic, educators have effectively used online tools and digital platforms to deliver anatomy classes, showcasing the versatility and adaptability of digital technologies in anatomy education (Attardi et al., 2022). In addition, digital technologies, such as augmented and virtual reality, have provided immersive and interactive learning experiences in anatomy education (Jiang, 2024).

Furthermore, combining art and science in anatomy education has been recognized as a valuable tool for developing scientific imagination and engaging students from diverse backgrounds. By incorporating visual arts into the science curriculum, educators can stimulate creativity, critical thinking, and interdisciplinary learning, ultimately enriching the educational experience for students (Okwara & Pretorius, 2023).

Finally, the importance of inclusivity in anatomical science education cannot be overlooked. An inclusive approach ensures that all students, regardless of their background, gender identity, or abilities, have equal access to learning opportunities and resources. By fostering inclusivity, educators create a supportive and wel-

coming environment that values diversity and promotes equity in education (Longhurst, 2024). This inclusive approach helps students develop a deeper understanding of anatomical variations and fosters a more inclusive and respectful attitude towards diverse patient populations in their future medical practice (Štrkalj & Pather, 2020).

In conclusion, the future of anatomical science education is moving towards a more integrated, inclusive, and technologically advanced approach that complements established practices such as cadaver dissection or prosection. By adapting to changing educational needs, embracing diversity, and providing adequate support for educators, anatomical science education is well-positioned to meet the demands of modern medical practice and ensure a high standard of anatomical training for future healthcare professionals.

The articles devoted to anatomical education published in this issue and the next issue represent evidence of Italian anatomists' attention to these issues.

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Two hundred years of the *Anatomia universa* of Paolo Mascagni (1755-1815): a milestone in the history of medicine and an innovative and modern approach to medical education

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Abstract. Two hundred years ago, the first of the nine volumes of Paolo Mascagni's *Anatomia universa* was published posthumously. This work was the fruit of a project that had occupied Mascagni for most of his life: an Atlas of anatomy that was the perfect replica on paper of dissection, a fundamental part of the teaching of this discipline. Through a short journey that traces some of the most important passages in the life of the great anatomist, the authors commemorate the *Anatomia universa*, an extraordinary work in the history and teaching of medicine. To do so, they draw on information and recover evocative *Anatomical plates* that are still conserved intact today in the prestigious Museum of Siena. The plates are organized to reveal the body from the superficial muscle layer down to the skeleton, as in the process of dissection. For the first time in the history of anatomy, the plates were life-size. Furthermore, in an original manner, and again for the first time, these plates showed the network of lymphatic vessels that Mascagni had brought to light a few years earlier. The beauty and perfection of these drawings are the result of Mascagni's knowledge and his ability to recruit the most expert artists and engravers of the time. Mascagni's treatises testify to the modernity of his approach to medical education, and his deep conviction that the main objective was to educate young people and to enable them to acquire the most perfect knowledge of the structure of the human body.

Keywords: Paolo Mascagni, *Anatomia universa*, history of medicine, medical training, teaching aids, anatomical tables.

INTRODUCTION

On 19 October 1815, while at home in Castelletto, near Siena, Paolo Mascagni (1755-1815) was struck by a pernicious fever. He died within a

few days, leaving his final works - *Anatomy for Scholars of Sculpture and Painting*, *Prodrome of Great Anatomy* and *Treatise on Anatomy for Medical Students* - partly complete and partly to be revised and printed. Paolo Mascagni summarized the figure of the scientist of his time, divided between rationalism of the Age of Enlightenment, development of scientific knowledge and the importance of agriculture, hopes in the new systems of government. All inserted in an era of revolutions and restorations. He was one of the most significant figures of his time so much so as to deserve a statue, commissioned by Ferdinand III of Lorraine, one of the great Tuscans, in Florence in the Uffizi square. He became famous for being the first anatomist to describe the lymphatic system in detail and to be the author of the first 'modern' anatomical atlas, conceived with didactic intent.

PAOLO MASCAGNI, "PRINCE OF ANATOMISTS" AND "INVENTOR OF THE LYMPHATIC VESSELS" [1]

Paolo Mascagni was born in Pomarance (Pisa) in 1755 to Aurelio Mascagni and Elisabetta Burrioni, both of whom belonged to ancient Sienese families.

He attended courses in philosophy and medicine at the University of Siena, but his knowledge went well beyond the boundaries of the medical disciplines; he was also particularly interested in *mineralogy, chemistry, and agricultural sciences*, as demonstrated by the numerous books on these subjects in his library.

Mascagni graduated in medicine in 1778 and, in the same year, became the assistant of Professor Pietro Tabarrani (1702-1780), a man particularly dedicated to studying organ pathology, and maintained constant scientific contact with Giovan Battista Morgagni (1682-1771), the "father of modern pathology" [2,3]. On the death of his mentor Pietro Tabarrani, on 4 April 1780, Mascagni was appointed Professor of Anatomy at the University of Siena, on the wishes of the Grand Duke Leopold II.

Even before graduating, Mascagni had started studying the lymphatic vessels on the invitation of Tabarrani. By injecting mercury (*Hydrargyrum*), he succeeded in highlighting the entire lymphatic network, its organization and its functions and alterations. In particular, he conducted his studies on subjects who had died in a state of anasarca (generalized massive edema), which is characterized by the accumulation of liquids in the interstitial spaces of the tissues and in the serous cavities; this enabled him to better visualize the lymphatic vessels, which were dilated as a result of the pathology.

This study was published in 1787 under the title of *Vasorum lymphaticorum historia et ichnographia* [4,5], the first description of the network of the lymphatic system. The text was accompanied by 27 plates drawn by the artist Ciro Santi, 14 counter-plates or linear plates, and the Catalogue of the anatomical preparations carried out in Florence to enrich the Grand Duke's collections.

Thus, Mascagni left aside clinical study and dedicated his entire life exclusively to the study and teaching of anatomy, which he considered a fundamental discipline in medical education. He taught anatomy at the University of Siena until 1800 and, by a decree of 1 January 1801, was appointed Professor of Anatomy at the University of Pisa, with the obligation to hold his lessons on anatomy, physiology and chemistry at Santa Maria Nuova Hospital in Florence, where a medical-surgical school was operative.

Immediately after the publication of the *Vasorum lymphicorum*, Mascagni began to conceive a new and particularly important project: "to exhibit by means of new plates, all the parts of the human body, and to present them precisely as they are in nature, with each retaining its proper order and position" [6].

Anatomy cannot be studied without a visual aid, whether it be a dissected body, a specimen, a model or drawing [7,8]. Moreover, the key phase of its teaching is dissection, which takes the form of a "representation" in a specially built facility, so that many spectators can observe the event. And from the theater - a word derived from the Greek *theàomai*, "I watch" - this facility took its name and purpose, becoming known as the "anatomy theater".

Over the centuries, however, as bodies on which to study were not always available, teaching aids such as anatomical plates were created. It was in this context that Mascagni conceived his *Anatomia Universa*, which virtually reproduced a dissection (9, 10).

His new anatomical Atlas was intended to describe the entire structure of the human body and became an innovative teaching aid for medical students when they could not practice directly on a corpse.

Mascagni represents the medical entourage of his time, which profoundly influenced the future of the scientific world, and which implemented the fusion between the theoretical teaching of medicine and practical activity. Mascagni defines the modern professor of medicine: far from both the physicist-philosopher and the empirical-practical of the past, he is a teacher deeply trained in biological disciplines, also made of physiology, pathological anatomy, and clinical, as evidenced by the multidisciplinary richness of Mascagni's treatises.



Figure 1. 19th century portrait of Paolo Mascagni: drawing by Roberto Focosi, engraving by Luigi Rados (Accademia dei Fisiocritici – Siena).

THE POSTHUMOUS WORKS OF PAOLO MASCAGNI

In 1815, at only 60 years of age, Mascagni suddenly died. This was also the beginning of the extremely controversial period in which his works were published. The climax came exactly 200 years ago, when, in 1823, the first volume of the *Anatomia Universa* was published. But the pathway to publication of his greatest work was far from smooth.

At the time of Mascagni's death, his *Anatomy for Scholars of Sculpture and Painting* [11] was almost ready for printing, and in 1816, just a year later, was published by his heirs – his brother Bernardino and his nephew Aurelio – who bore the costs.

The scientific aspects were handled by Mascagni's last dissector, Francesco Antommarchi (1780-1838), who in 1819 became Napoleon's personal doctor during his exile on Saint Helena. The text was accompanied by 15 plates featuring human figures posing, as if during a real-life drawing lesson, as the work was intended for the teaching of anatomy in art institutes.

In 1819, a limited company, established by Mascagni's family for the purpose of publishing his works, published the *Prodrome of Great Anatomy* [12] in a very rich folio edition.

- The first volume consisted of the following chapters: *Lymphatic vessels; Blood vessels; Nerves; Muscles; Ligaments and cartilages; Bones; Lung; Liver; Alimentary tracts.*
- The second volume comprised 20 plates, drawn and engraved by Antonio Serantoni (1780-1837), featuring images obtained from microscopic observation and particularly detailed macroscopic images.

More than an introduction to the main work, which had not yet been published, it was a text on anatomy and histology, and contained several references to physiology and pathological anatomy, the latter being an acknowledgment of the training received from Pietro Tabarrani. In this case, too, the scientific aspects were handled by Francesco Antommarchi.

Regarding the *Prodrome of Great Anatomy* [12] the innovative nature of Mascagni's work is noteworthy – as also explained in the five pages of the “Publisher's Preface”. Indeed, Mascagni represented the human body by starting from the superficial layer and not from the skeleton, as was normally the case at the time, indicating that anatomical works should represent a sort of dissection on paper.

In this respect, Mascagni distinguished himself from previous anatomists, who had adopted the approach prescribed by Leon Battista Alberti (1404-1472) in his *De Pictura*: “just as we dress a man, we first draw him naked, then we clothe him; thus, to paint the nude, we first place his bones and muscles, which we then cover with his flesh, so that it is not difficult to understand where each muscle is underneath” [13].

Two years later, in 1821, a second edition of the *Prodrome of Great Anatomy* [12] was published, again in two volumes, but this time in octavo format. Scientific editing was entrusted to Tommaso Farnese.

That the relationship between the Mascagni's family and Francesco Antommarchi had soured is demonstrated by what Farnese wrote at the beginning of the new edition of the *Prodrome* in his dedication to Professor Andrea Vaccà-Berlinghieri (1772-1826), a friend and great admirer of Mascagni: “I prepared to illustrate and publish the deceased author's genuine text of the *Prodrome*, purged of the excessively free variations made by a compiler”.

Early in 1822, Antommarchi obtained a court order to dissolve the limited company and disappeared. Mascagni's family sold his manuscripts, drawings and copper engravings to three professors of the University of Pisa – the above-mentioned Andrea Vaccà-Berlinghieri, Giacomo Barzellotti (1768-1839) and Giovanni Rosini (1776-1855) – so that the *Great Anatomy*, on which the Sienese anatomist had worked for decades, could be published. Translated into Latin, it was entitled *Anatomia*

universa and published in nine volumes, issued one per year from 1823 to 1831.

Meanwhile, Francesco Antommarchi plagiarized Mascagni's work. When he moved to Saint Helena to join Napoleon, he took with him the notes and writings prepared by Mascagni for the great atlas and some print drafts of the anatomical plates.

Between 1823 and 1826, in Paris, he published this material, which he had revised, "passing off these works as his own" [15] and "having some plates engraved in lithography by using the proofs from the copper engravings" [10]. The ensuing situation was very complicated, but in the end, Paolo Mascagni was recognized as the true author of the work.

THE ANATOMIA UNIVERSA

Dedicated to Grand Duke Leopold II, this work consisted of a part of text in small folio, the *Anatomia universa*, and a 44-plate atlas, the *Anatomiae universae Pauli Mascagnii icones* (Fig. 2), in the maximum folio format.

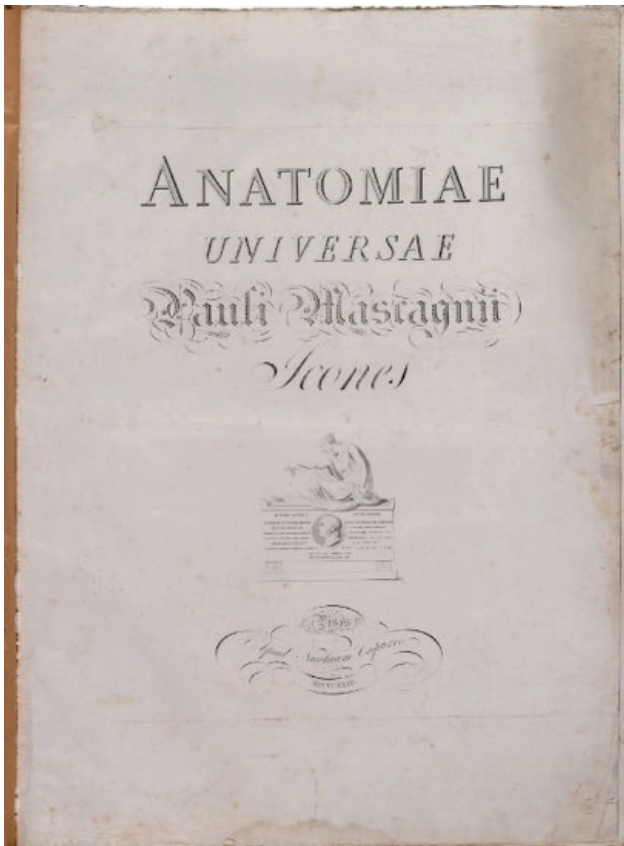


Figure 2. Paolo Mascagni, *Anatomiae Universae Pauli Mascagnii icones*, 1823-1832.

The plates of the *Anatomia universa* were prepared by means of etching. A copper matrix was covered with black wax, on which the image to be printed was drawn. The matrix was then incised so as to leave the copper exposed in correspondence with the drawing. Subsequently, a mixture of nitric acid and water was poured over the matrix to corrode the parts that had been stripped of wax.

The principle of this technique is based on the protective power of black wax and the corrosive power of nitric acid. Once cleaned, the plate was ready for printing like a normal intaglio. Successive passages over the same matrix allowed further inking with different colors; for this reason, etching was better suited to color printing than burin engraving [16]. Thanks to this technique, as well as to the skill of the artists and engravers, Mascagni's plates are not only extraordinary in their precision and richness of detail, but they are also beautiful.

Mascagni's cenotaph is shown on the frontispiece of the work (Fig. 3); sculpted by Stefano Ricci, the cenotaph is preserved in Siena, at the Accademia dei Fisiocritici, where the University has deposited Mascagni's archival and book heritage and some of the preparations made for his first work, *Vasorum lymphaticorum historia et ichnographia*.



Figure 3. Marble cenotaph to Paolo Mascagni, with the personification of Anatomy mourning the loss of her teacher (photograph, Davide Orsini).

The originality of the *Anatomia universa* and its importance in the field of medical training stem from Mascagni's completely new vision of the tools that could enhance students' understanding of anatomy even in the absence of dissection, which at that time was fundamental and indispensable.



Figure 4. Paolo Mascagni, *Anatomia Universa*, *stratum primum*, *facie adversa* (Sistema Museale Universitario Senese).

In his work, Mascagni depicts the human body as seen frontally (*facie adversa*) and from the back (*facie aversa*), as on the dissecting table. Twenty-four plates (102 cm length, 75 cm width) are designed in such a way that, when arranged 3 to 3 vertically, they show life-size human bodies: an absolute novelty in the field of anatomical publishing (Fig. 4).

The human body is represented according to stratigraphical criteria, “*per diversa strata a cute ad sceletum*” (“through different layers, from the skin to the skeleton”): the first layer (“*stratum primum*”) illustrates the human figure deprived of skin and shows superficial muscles, nerves and vessels; the second layer (“*stratum secundum*”) depicts muscles, nerves and deep vessels, while the third (“*stratum tertium*”) reveals muscles, arteries and veins of the deeper layer down to the skeleton (“*stratum quartum*”).

These representations of the human body are followed by 20 plates illustrating viscera and various other organs, again in life size (Fig. 5).



Figure 5. Paolo Mascagni, *Anatomia Universa*, *Viscera*, *tabula I* (Sistema Museale Universitario Senese).

Mascagni's tables are absolutely perfect, as every detail was meticulously verified by the anatomist himself through hundreds of dissections; moreover, they were created by very talented artists and engravers: Ciro Santi in the case of *Vasorum lymphaticorum historia et ichnographia* and Agostino Costa and Antonio Serantoni for the *Anatomia Universa*.

Mascagni was meticulously attentive to the quality of the plates for his great *Atlas of anatomy* and determined to safeguard their beauty. Therefore, in addition to the 44 principal plates, he also commissioned 44 counter-plates showing only the outlines of the figures and the letters and numbers that refer to the captions. Thus, he was able to avoid spoiling the beauty and readability of the images in any way.

Mascagni's two anatomical atlases therefore mark the culmination of his life and professional work. In particular, the *Anatomia universa*, on which he worked for about 30 years, is extraordinary on account of its depiction - and this was the first time in history - of the lymphatic system. In it, his greatness as a scholar and as a teacher of anatomy is evident.

CONCLUSIONS

The publication of the *Anatomia universa* two centuries ago was a veritable milestone in the history of medicine and in the teaching of anatomy.

Paolo Mascagni's contribution to the teaching of anatomy is still considered fundamental today, thanks to his skill in evaluating and synthesizing the anatomical knowledge of the past and of his own era through the constant and meticulous practice of dissection. His great ability to conceive and create essential teaching aids to the study of the human body also stemmed from his ability to combine art and science.

The medical science of the eighteenth century and then even more of the nineteenth century is renewed, relying increasingly on an Anatomy that was direct analysis of the body through systematic anatomical investigations on the corpse, explaining the essence of the disease and no longer the only symptom. The new anatomical science supports clinical reasoning, making use of the contributions of other disciplines designed to constitute the modern teaching programs of the medical faculties, establishing a close link between the university and the hospital.

More than two centuries after his death, Mascagni is remembered not only for his fundamental work in the anatomical field, but also for his innovative teaching method and the outstanding quality of the tools that he created for the teaching and study of anatomy. Convinced

of the indispensable role of dissection and the direct observation of bodies in the study of medicine, Mascagni demonstrated this concept through the mediation of the anatomical plates of his *Anatomia universa*, which are as perfect as they are innovative in their 1:1 ratio.

Thus, Paolo Mascagni's *Anatomia universa* remains a truly unique work in the history of medicine, a perennial testimony to his extraordinary determination to contribute to the formation of a new medical class, in line with his unshakeable conviction that his main objective was to educate young people and to ensure that they acquired the most perfect knowledge of the structure of the human body.

NOTES ON CONTRIBUTORS

Davide Orsini: Conceptualization (equal); writing – original draft (equal); review and editing (equal). Maria-no Martini: Conceptualization (equal); writing – original draft (equal); review and editing (equal). Daniele Saverino: Conceptualization (supporting); review and editing (equal). Anna Siri: Conceptualization (supporting); review and editing (equal).

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Evaluating the effectiveness of drawing as a pedagogical tool in teaching histology and human anatomy to dental and allied health sciences: a three-year observational study

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Abstract. Anatomical sciences are visual sciences that deal with the structure at gross and microscopic levels. Throughout history, drawing has served as a prominent tool for learning and teaching anatomical sciences, tracing back to notable figures such as Claudius Galen, Andreas Vesalius, Leonardo Da Vinci, and Henry Vandyke Carter's illustrations in Gray's Anatomy among others. In this observational pilot study spanning over three years, we investigated the efficacy of utilizing drawing as a pedagogical tool for learning histology and human anatomy. This study involved 201 participants comprising dental, and allied health sciences. Pre- and post-activity surveys were administered to assess students' perceptions and attitudes towards incorporating drawing as an adjunctive method for teaching and learning structural sciences, particularly histology and anatomy. Analysis of the survey data revealed a significant level of appreciation and interest in the drawing approach, with 80% of participants expressing a positive inclination towards its future integration into educational practices. The significance of drawing as a pedagogical approach for anatomical sciences, drawing upon insights from previous research and observations gleaned from our surveys. In conclusion, on this basis we recommend further development and implementation of drawing-based teaching methodologies in future educational contexts.

Keywords: teaching, anatomy, histology, drawing.

PREAMBLE

This study was conducted under the guidance of Professor Abdo Jurjus, Professor of Anatomical Sciences at the American University of Beirut. Professor Jurjus emerged as one of the pioneering anatomists within Mediterranean universities to recognize the existing challenges in the teaching of morphological sciences. He advocated for a critical review of teaching methodol-

ogies, particularly given the prevalent absence of practical exercises in histology laboratories and gross anatomy classrooms in many universities. For more than four decades, Professor Jurjus initiated an innovative, interactive approach to teaching within his anatomy courses to medical and paramedical students at the American University of Beirut. Given his expertise and innovative teaching methods, our research group deemed Professor Jurjus as the most suitable individual to provide guidance and mentorship for our study in this domain.

INTRODUCTION

Over the centuries, the integration of art into scientific disciplines has demonstrated its significance as a valuable educational tool for teaching and learning morphological sciences, particularly visual sciences like anatomy and histology. Despite its deeply rooted historical utilization within medical education for the study of the human body and its structures, the role of drawing art has somewhat diminished in modern dental and medical curricula (Goetz, 1991). This oversight is notable, especially within fields like dentistry, “Art Dentaire” as used to where students engage in cosmetic procedures that demand acute observation of intricate details. Dentists rely heavily on manual dexterity, color and pattern recognition, and visual acuity to discern clinical examination findings, establish diagnoses, and execute aesthetically pleasing dental restorations. Research suggests that exposure to fine art not only fosters clinicians’ intellectual curiosity and critical thinking but also enhances diagnostic skills and cultivates empathy towards patients (Katz & Khoshbin, 2014; Schaff, Isken & Tager, 2011; Shapiro, Rucker & Beck, 2006). Concurrently, amidst the rapid advancements in information technology, visual art has been proposed as an effective pedagogical tool for learning sciences, particularly in the realm of structural and anatomical sciences such as histology and anatomy (Elmongi, 2019). The impact of visual aids, including pictures, on learning and knowledge retention has been the subject of numerous previous research endeavors, consistently demonstrating positive outcomes when pictorial elements are incorporated into relevant teaching materials (Alesandrini, 1981; Alesandrini, 1984; Larkin & Simon, 1987; Vorstenbosch et al., 2013). The cognitive processes underlying the beneficial effects of images and audiovisual strategies on text comprehension have been explored extensively. Glenberg and Langston (1992) conducted a series of experiments to assess these effects, revealing that pictures facilitate the construction of mental models by learners, thereby improving the retention of learned material (Balemans et

al., 2016). Further investigations into this phenomenon led Mayer and Anderson (1991) to propose the integrated dual-code hypothesis, positing that learners construct both visual and verbal mental models and establish connections between them. In this study, we present a pilot observational investigation into the utilization of drawing as an educational tool for learning human anatomy and histology among dental and allied health sciences students. Our aim is to assess students’ perceptions and attitudes towards this approach and to explore its potential for future development and reintegration into histology and anatomy teaching strategies.

MATERIALS AND METHODS

One hundred ninety-nine first-year students, 25 on the first year, 80 on the second year and 94 on the third year enrolled in the School of Medicine at the University of Palermo in Italy, comprising students from the following fields: dental, dietitian, neurophysiopathologists technicians, and prevention technicians in the workplace. Students voluntarily participated in this study, they were concurrently attending the Human Anatomy and Histology module as part of their curriculum. The module, inclusive of Human Anatomy, Histology, Cytology, and Embryology, constitutes an integral component of the first-year dental curriculum and is mandatory for progression to oral examination assessments. The Human Anatomy module encompasses the study of various systems, while the Histology module encompasses units such as General Histology and Cytology. Participants were invited to partake in this observational pilot study during designated free learning hours. They were requested to bring their preferred drawing materials, including paper and pencils.

During the study, students were tasked to draw a histological or anatomical structure of their choosing, focusing on cellular structural elements such as organelles, tissues, or organs. The activity spanned over a duration of three hours, during which participants were granted complete autonomy in selecting their preferred drawing style and techniques. Notably, the workshop was conducted subsequent to the delivery of the Anatomy and Histology (Cytology) content, assuming an optimal level of familiarity with cytological structures among participants.

Upon completion of the workshop, all drawings were collected for further analysis, as depicted in Figures 1 to 9.

Pre-activity and a post-activity survey were conducted among the participants. In the pre-activity survey 3 questions were asked. These questions covered the

(1) willingness to participate and explore new learning methods, (2) could drawing interest you as a new learning tool to study histology, cytology, and gross anatomy, (3) whether the participant already had experiences where drawing was used to learn science topics.

Similarly, 3 questions were asked in the post-activity survey. They covered (1) the interest in this artistic experience, (2) usefulness of the workshop to learn histology, cytology, and gross anatomy, and lastly (3) if art should be integrated in such learning.

RESULTS

Observation and Reflection on Conducted Surveys:

A total of 199 students actively participated in the workshop, contributing their artwork, and diligently responded to both pre- and post-workshop surveys. Surveys were conducted anonymously to safeguard participant privacy, and no personally identifiable information

was collected. The pre-workshop survey aimed to assess students' perspectives and interest in utilizing drawing as a learning tool, as well as their prior exposure to this instructional method.

Conversely, the post-workshop survey aimed to evaluate students' appreciation of the artistic activity, their perception of its effectiveness in enhancing histology learning, and their likelihood of recommending such activities as an integrated component of gross anatomy and histology teaching.

A summary of students' responses to the pertinent survey questions is provided in Table 1.

Figure 1 shows data from the pre-activity survey over 3 years in response to the 3 questions: (1) willing to explore the new learning method, (2) expressing interest in the learning tools for anatomical sciences, and (3) if the student had experiences using artistic drawings to learn science. In the year 2021, 92% of the students were willing to participate in the survey and explore new learning methods, and 100% were inter-

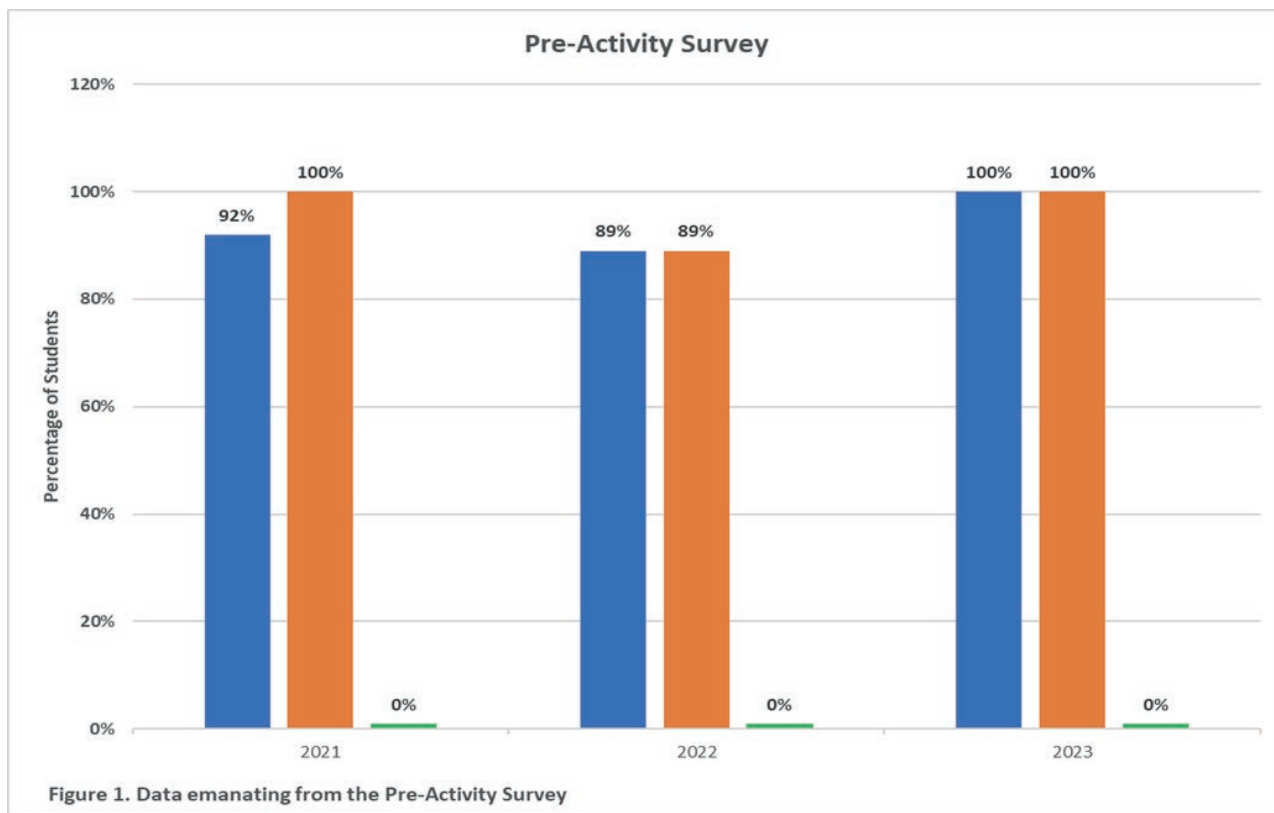


Figure 1. Data emanating from the Pre-Activity Survey

- Question 1: Would you be willing to participate in and explore new learning methods?
- Question 2: Could drawing interest you as a new learning tool to study histology, cytology, and gross anatomy?
- Question 3: Have you already had experiences where artistic drawing was used to learn science topics?

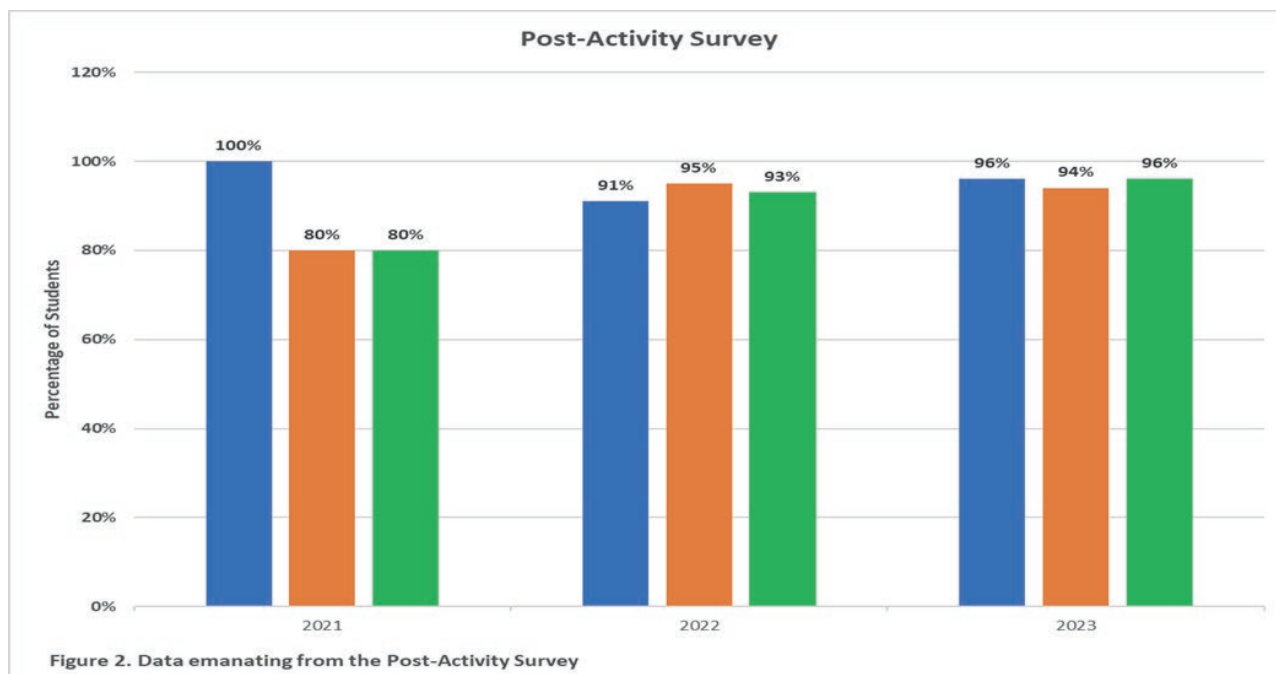
Figure 1.

Table 1. Summary of the data collected over 3 years.

Pre-activity survey questions	Post-activity survey questions
First Study 2021	
Would you be willing to participate in and explore new learning methods? Yes: 23/25 (92%) No: 02/25 (8%)	Did you find the artistic experience interesting? Yes: 25/25 (100%) No: 00/25 (0%)
Could drawing interest you as a new learning tool to study histology/ cytology and gross anatomy? Yes: 25/25 (100%) No: 00/25 (0%)	Was the organised drawing workshop useful to learn histology/ cytology and gross anatomy? Yes: 20/25 (80%) No: 05/25 (20%)
Have you already had experiences where artistic drawing was used to learn science topics? Yes: 0/25 (0%) No: 25/25 (100%)	Should art be integrated as a tool for histology/cytology learning? Yes: 20/25 (80%) No: 05/25 (20%)
Second Study 2022	
Would you be willing to participate in and explore new learning methods? Yes: 71/80 (88,75%) No: 09/80 (11.25%)	Did you find the artistic experience interesting? Yes: 73/80 (91.28%) No: 07/80 (08,72%)
Could drawing interest you as a new learning tool to study histology/ cytology and gross anatomy? Yes: 71/80 (88,75%) No: 09/80 (11.25%)	Was the organised drawing workshop useful to learn histology/ cytology and gross anatomy? Yes: 76/80 (95%) No: 4/80 (05%)
Have you already had experiences where artistic drawing was used to learn science topics? Yes: 0/80 (0%) No: 80/80 (100%)	Should art be integrated as a tool for histology/cytology learning? Yes: 74/80 (92,50%) No: 6/80 (07,50%)
Third Study 2023	
Would you be willing to participate in and explore new learning methods? Yes: 94/94 (100%) No: 0/94 (00%)	Did you find the artistic experience interesting? Yes: 90/94 (95,74%) No: 04/94 (04,25%)
Could drawing interest you as a new learning tool to study histology/ cytology and gross anatomy? Yes: 94/94 (100%) No: 0/94 (00%)	Was the organised drawing workshop useful to learn histology/ cytology gross anatomy? Yes: 88/94 (93,61%) No: 06/94 (06,38%)
Have you already had experiences where artistic drawing was used to learn science topics? Yes: 00/94 (00%) No: 94/94 (100%)	Should art be integrated as a tool for histology/cytology learning? Yes: 90/94 (95,74%) No: 04/94 (04,25%)

ested in drawing as a new tool to learn, however none of them has had any previous experience in drawing as a tool for learning science topics. In the year 2022, 89% were willing to explore this new method of learning, and the same percentage also were interested in this

new learning tool, again none of them had prior experience to artistic drawing as a learning tool. This percentage increased in the year 2023 in which 100% were willing to participate and explore the use of artistic drawings as a new learning tool for scientific topics, although



- Question 1: Did you find the artistic experience interesting?
- Question 2: Was the organized drawing workshop useful to learn histology, cytology, and gross anatomy?
- Question 3: Should art be integrated as a tool for histology, cytology learning?

Figure 2.

none of them had previous experience in artistic drawing as a learning tool.

In Summary, practically all the populations in the 3 years were consistently willing and enthusiastic to participate in the new teaching and learning method, from 89% to 100% of students.

On the other hand, in Figure 2 the data showed the response of students to the post-activity questions in the same 3 years 2021, 2022, and 2023. In this survey, all of them (100%) did find that this artistic experience was interesting in the year 2021, while 91% in 2022, and 96% in 2023. In contradistinction, only 80% of the students in the year 2021 found this workshop useful in the learning of histology, cytology, and gross anatomy, and the same percentage (80%), think that art should be integrated as a learning tool for histology, cytology learning. Data in the year 2022 was also close. The results showed that 91% found the artistic experience interesting, while 95% found it useful as a learning tool for histology, cytology, and gross anatomy, and 93% think that art should be integrated as a tool for, histology, cytology and anatomy learning. In the year 2023, the greatest majority, close to 100%, found this experience interesting, 94% found the workshop use-

ful for learning, and 96% think that artistic drawings could be integrated as a learning and teaching tool for anatomical sciences.

In Figure 3, the authors selected 9 representative drawings performed by the students. In brief, the drawings indicated the level of retained knowledge by the students to construct and reproduce the microstructure of subcellular components (1-4), the histological microscopic details of tissues and organs like esophagus (5), skin (6), stomach (7), large intestines (8), and the brain (9)

A closer look at the drawings will enable the instructor to evaluate the effectiveness of the drawings in reflecting the degree of achievements by the students in grasping the learning student outcomes relevant to the course objectives and to the expected competencies to be achieved by the end of the learning sessions. It is believed that the photos convey clearly the message that the students retained optimal knowledge, improved their skills in reproducing the acquired knowledge and in expressing a positive attitude towards this learning approach and teaching strategies.

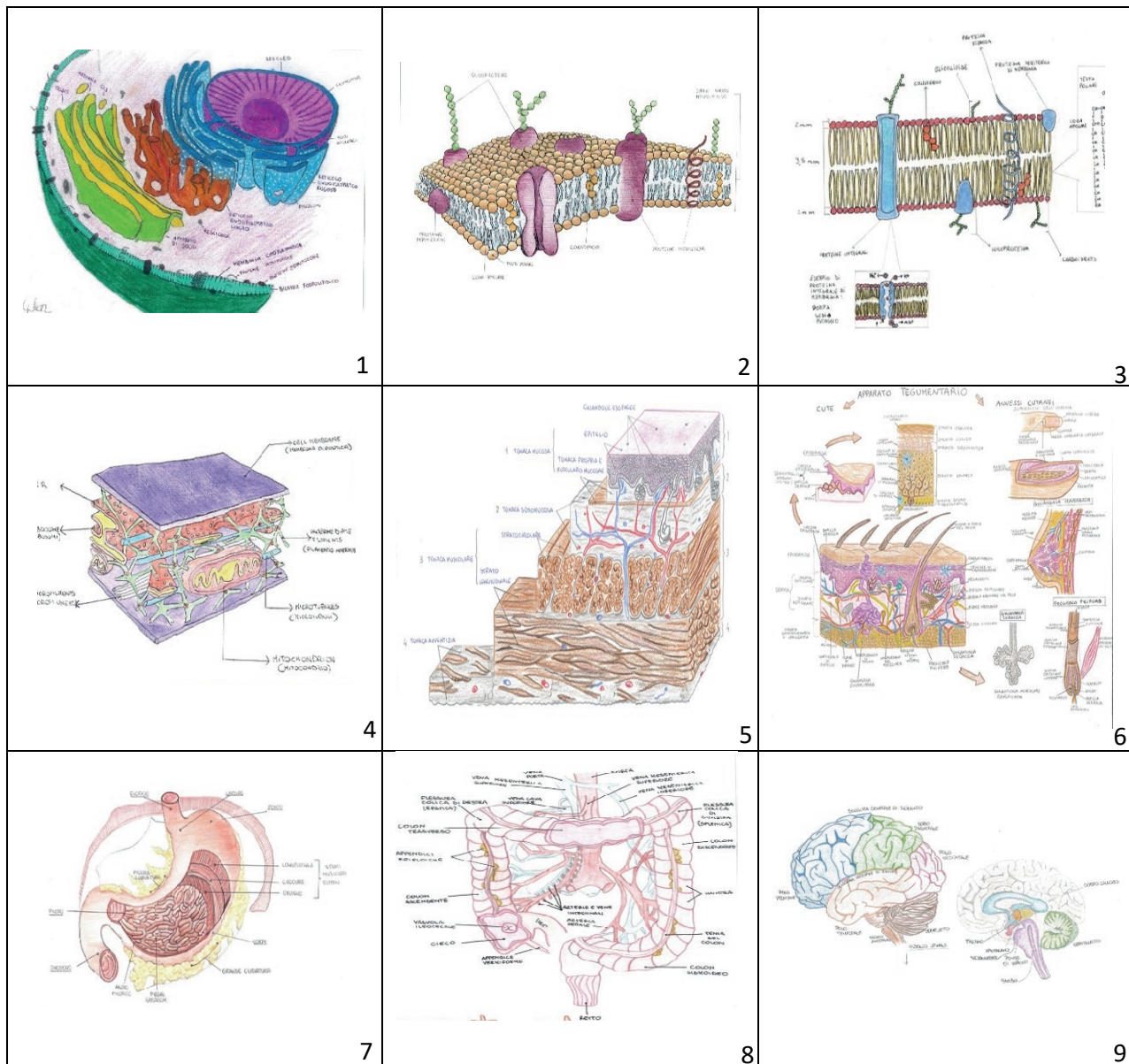


Figure 3. Selected drawings prepared by the targeted students covering Cytology, Histology and Gross Anatomy. The identity of the students were hidden.

DISCUSSION

Data in this study show clearly with a significant agreement from the students over the 3 year period that teaching and learning by drawing could be considered as an optional methodology among our teaching strategies in anatomy despite the booming advances in information technology and the availability and accessibility of students to interactive audiovisual educational programs, teaching and learning by drawing could have a

place as an adjunct teaching resource next to the cadaver, the original source of information.

In multiple occasions, in the dissecting room, students go to the white or black board to make drawings of the region being dissected and make the effort to reproduce and discuss what they discovered in the cadaveric specimens among the team members. Making such drawings constituted an excellent resource to share and discuss among the students in the team, thus promoting interaction, team work, and enhancing profes-

sionalism among colleagues, future medical and paramedical graduates.

For those of us who had their anatomy before the seventies of the last century, in the American and especially in the European curricula, drawings were used and considered as an essential tool to learn anatomy. However, teaching our students human anatomy in the last 50 years has moved away significantly from drawings. The prime movers of such changes were the constraint of time allocated to anatomical sciences and the booming of the audio visual, information technology-based programs.

In conclusion, such preliminary data shed light on the potential positive role of using drawing in our teaching strategies. The use of computers, tablets and even all phones could make such drawings fast, accessible, and more useful as learning and teaching tools.

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Anatomical education and its innovations: an interdisciplinary, hands-on, team-building approach

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Abstract. Contemporary approaches in anatomical education, such as problem-based learning, case-based learning, and the flipped classroom, grounded in evidence and tailored to student needs, have demonstrated marked enhancements in student engagement and interactions. These methodologies shift the educational focus from passive knowledge transmission to active knowledge construction by students, fostering task-oriented learning. This inquiry explores the implementation of a dynamic, multimodal, and engaging learning approach to teach second-year MBBS students about musculoskeletal and splanchnic anatomy at the School of Medicine, The University of Bari 'Aldo Moro', Bari, Italy. Additionally, it investigates student perceptions regarding anatomy learning and traditional lectures, along with their views on participating in problem-based learning sessions. In these problem-based learning sessions, small groups of students engage in discussions, formulate hypotheses, establish learning objectives in anatomy, and virtually dissect human bodies using the Anatomage Table. This innovative approach provides a comprehensive view of the anatomy of the body region, aiding the exploration of structures relevant to the symptoms presented by patients described in the problem-based learning sessions. The academic performance of students exposed to active learning is compared with that of their more traditionally taught counterparts. Our findings underscore the efficacy of employing an active, multimodal, and engaging learning strategy based on Anatomage-enhanced problem-based learning as a potent additional tool in anatomy education. To further validate these outcomes, future research endeavors should include randomized controlled trials, aiming to assess the comparative effectiveness of different learning strategies that have the potential to advance medical education.

Keywords: anatomy, student-centred learning strategies, active and engaging learning, medical education, multimodal approach.

INTRODUCTION:

The Medicine and Surgery degree program aspires to equip students with a comprehensive set of the knowledge and skills, both technical and non-technical, demanded by society. The goal is to mould them into capable and confident medical practitioners or surgeons upon graduation. However,

in today's era characterized by rapid innovation, intense specialization, and heightened scrutiny of medical liability, ensuring students' proficiency in both technical and non-technical aspects poses a formidable challenge.

Numerous multicenter studies reveal a prevailing lack of readiness among medical and surgical graduates to independently execute fundamental procedures (Borman et al. 2008, Cardenas Lara et al. 2017, Coleman et al. 2013, Ellis 2001, George et al. 2017). The expanding role of simulation and augmented reality in learning is evident, yet, as reiterated in research studies (Mc Garvey et al. 2001, Moro, Smith, and Stromberga 2019, Rajeh et al. 2017, Theodoulou et al. 2020), nevertheless the most effective approach for medical degree courses still remains the multimodal-multidisciplinary approach. A progressive immersion in the field of medical knowledge through the use of different methods and stimuli ensures a contemporary and comprehensive training experience. In understanding human diseases, Mondino da Liuzzi's 1316 insight on anatomical dissection remains pertinent: "...the senses of touch and sight can be used to improve understanding of the human body. You can actually see and feel the structures moving under the skin." Human anatomy, rightly regarded as the cornerstone of medical knowledge, underpins competent and safe clinical practice, especially in surgical disciplines and advanced technological therapies like the modulation of neuronal activities through brain micro-electrode implantation (Camp et al. 2016, Estai and Bunt 2016, Hu, Wattchow, and de Fontgalland 2018, Jeyakumar, Dissanayake, and Dissabandara 2020, Morris and Jacques 2018, Nazarali et al. 2019, Megevand et al. 2017).

Anatomical education has changed profoundly over the last few years. Sometimes, students seem less responsive and show little enthusiasm towards what they study. This is probably due to a new generation of students who learn differently from those of past years (Eckleberry-Hunt, Lick, and Hunt 2018). The coronavirus pandemic has greatly influenced some of the most sensitive members of society: young people and their mental health (Calbi et al. 2021). Isolation and even an excessive exposure to social media have sometimes caused a state of malaise (Gao et al. 2020, Karim et al. 2020). Nowadays students no longer tolerate anymore the classic didactic frontal lectures in which they usually take notes rather passively and with poor interactions with one other (Freeman et al. 2014). This tendency has made it necessary to adopt new methods and effective strategies in anatomical education in order to involve students and keep them as interested as much as possible (Singh et al. 2019). Numerous potent strategies and resources exist for instructing anatomy. While

conventional approaches hinge on didactic lectures and exhaustive body dissection to impart topographical structural anatomy, the latter, although an exorbitant investment, remains a cornerstone. However, recognizing the financial constraints and the evolving landscape of education, virtual dissection has gained precedence in numerous medical schools. Its appeal lies in fostering independent learning and affording flexibility in scheduling. (Vasil'ev et al. 2023, Pasricha et al. 2023, Zhao et al. 2020, Bartoletti-Stella et al. 2021). Among different computer-based learning tools, the Anatomage Table 9.0 (Anatomage Inc., San Jose, CA, USA) offers a complete anatomical device for medical student education (Bartoletti-Stella et al. 2021).

Nevertheless, several experts advocate a discerning application of a dynamic multimodal-multidisciplinary approach. This encompasses dissection, lectures, small group discussions utilizing problem-based learning (PBL), case studies, and living anatomy. This holistic strategy facilitates meaningful connections with faculty instructors, peers, diagnostic imaging, and embraces the evolving landscape of human-to-human and human-to-machine interactions. Its inherent benefits are particularly pronounced in addressing the challenges posed by post-COVID-19 student isolation (Evans and Pawlina 2021, Xiao et al. 2020, Pabst and Rothkotter 1997, Marks 2000, Levine et al. 1999). Indeed, the pandemic-induced absence of social interactions, coupled with the detrimental misuse of social media, is bound to exert significant and adverse consequences, particularly within the professional sphere in the imminent future (Gao et al. 2020, Karim et al. 2020).

PBL has been demonstrated to enhance the integration of students' knowledge (Barrows 1986). Through clinical cases, students adeptly forge connections between clinical features and fundamental scientific concepts. Cognitive psychology affirms that the integration of knowledge not only facilitates retention but also enhances the subsequent retrieval of pertinent information. Along with other scholars, we assert that Problem-Based Learning (PBL) should be geared towards equipping students more effectively for real-world clinical practice. (Regehr and Norman 1996). In addition, case-based learning (CBL) and flipped classroom in Anatomy have been demonstrated to be more effective than didactic lectures for improving and retaining of knowledge (Sangam et al. 2021, Kazeminia et al. 2022)

In the era of competency-based medical education, instilling clinical reasoning skills becomes imperative even in the pre-clinical stages, notably during the second year of the medical curriculum. This demands a profound comprehension of imaging and three-dimensional

anatomy, pivotal factors for accurate diagnosis, differentiation, and secure patient treatment. (Darras et al. 2018). With a focus on these critical aspects, this study endeavours to assess the viability, acceptance, and efficacy of implementing a cutting-edge multimodal-multi-disciplinary approach to musculoskeletal and splanchnic anatomy learning. This approach is centred on virtual dissections utilizing Anatomage 9.0, case studies and flipped classroom lectures, along with small group discussions adopting Problem-Based Learning (PBL) methodologies. The aim is to enhance the teaching of gross and microscopic anatomy to medical undergraduates.

MATERIAL AND METHODS

The entire Human Anatomy 1 course, covering musculoskeletal and splanchnic anatomy from March 2023 to January 2024, was conducted at the University of Bari School of Medicine, encompassing all 151 students in the first and second years of the BSSM program. To progressively integrate a dynamic and engaging learning strategy, the course structure underwent progressive modification, featuring 40 traditional didactic lectures (66.6%), 5 flipped classroom sessions (8.5%) with 14 students as presenters, covering topics such as the temporal, sphenoid, maxilla, mandibular bones, urinary system, superficial anatomy and blood vessels of the neck, larynx. Additionally, there were 7 Case-Based Learning (CBL) sessions (11.6%; aortic dissection, acute cardiac tamponade, Lyme's disease, coronary artery lesions in Takayasu arteritis, tongue and oesophageal cancers, traumatic splenic rupture, anterior pituitary hypoplasia) and 6 Problem-Based Learning (PBL) sessions incorporating virtual dissections using Anatomage (13.3%; headache and transvers sinus thrombosis, unstable angina, pleural mesotelioma, lower urinary tract symptoms due to prostatic hyperplasia, cervical uterus cancer, Addison's disease).

The Anatomage Table version 9.0, a virtual table with four different cadavers providing a 3D spatial dissection view, played a pivotal role in enhancing PBL sessions. Learning materials for CBLs and PBLs involved clinical cases with specific anatomical questions, addressing areas like the aorta, heart, coronary arteries, iliac vessels, oesophagus, spleen, thoracic outlet, clavicle, hypophysis, tongue, transverse sinus, pleura, urethra, and prostate. In PBL, 66 students were divided into 6 groups with a tutor as a facilitator. The students analyzed case scenarios, discussed questions within their groups, and utilized textbooks and reference materials. Internet access was granted for additional resources and

the Anatomage table was used to visualize anatomical structures during case analysis. Anatomage descriptions were incorporated during the 5th phase of the Maastricht model of PBL (Schmidt 1983). The tutor guided discussions, provoked critical thinking, and summarized topics at the session's conclusion. Extra assistance was provided to students unfamiliar with virtual dissections on Anatomage.

Of the entire cohort, 66 students (44%, voluntary participation) actively participated in both two online feedback questionnaires (Ahaslides, phone-based: <https://ahaslides.com/>) assessing the quality, potential, and outcomes of teaching musculoskeletal and splanchnic anatomy using active learning methods such as PBL. The list of post-session multiple-choice questions used in the online tests is detailed in Table 1.

Table 1. Feedback survey questions posted to students after completing musculoskeletal and splanchnic anatomy.

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1. Do you find the PBL self-learning method useful?
 2. Is the PBL method of learning more interesting and useful than traditional lectures?
 3. Does the PBL method slow down studying for the anatomy exam?
 4. Was the PBL method perceived as overly challenging?
 5. Was the planning of the PBL considered well-executed?
 6. Did the PBL effectively stimulate group discussions?
 7. Did the PBL encourage independent learning?
 8. Did the PBL contribute to integrating various disciplines?
 9. Was there unanimous agreement within the group to adhere to the study topic?
 10. Did every student uphold the commitments they made within the group?
 11. Was the overall group climate considered pleasant?
 12. Did you acquire substantial knowledge from participating in the PBLs?
 13. Comparatively, did you learn more from traditional lectures than PBLs?
 14. Did the teacher effectively stimulate and motivate interest in the discipline?
 15. Do you prefer active teaching methods (PBL, case studies) with consistent student involvement?
 16. If yes, specify the type of teaching that satisfied you (PBL, case study, flipped classroom, etc.). Write freely.
 17. Would you be interested in actively participating in developing next year's program as a co-project?
 18. Are the supplementary teaching activities (Anatomage virtual dissections, peer tutoring, musculoskeletal laboratories, etc.) useful for learning the subject?
 19. Are you satisfied overall with how the exercises were set up?
-

* Choices for each question: 1) Definitely No; 2) More No than Yes; 3) More Yes than No; 4) Definitely Yes.

To gauge conceptual retention, we scrutinized the final scores of the Anatomy 1 examination within two distinct student cohorts. These cohorts underwent the examination utilizing identical methods, involving a multiple-choice test and Anatomage axial section description, followed by an oral examination encompassing microscopic and topographic anatomy. The assessments were conducted by the same two instructors during the initial three sessions at the conclusion of the course in two successive years (2023: 100% traditional teaching method and 2024: 67% traditional, 33% engaging students).

RESULTS

The instructional intervention reached the entire group of 151 students enrolled in the Anatomy course. Of this cohort, 66 students (44%) actively engaged in both online tests at the end of musculoskeletal and splanchnic anatomy.

Initial surveys conducted at the end of the musculoskeletal session revealed that 63% of students favoured an innovative educational approach with continuous engagement, while 42% preferred lessons supported by case studies. Others indicated a variety of preferences, such as Team-Based Learning (TBL), PBL, and flipped classrooms.

Subsequent surveys administered at the end of the anatomy course disclosed that 96% of students expressed a preference for innovative education, deeming it more beneficial and engaging than traditional frontal lectures. The same percentage acknowledged that PBL had stimulated group discussions, fostering an enjoyable teamwork experience. Additionally, 91% believed they had significantly learned from PBL, with 95% noting that the new method had promoted self-study, and 100% attesting that it facilitated an interdisciplinary perspective. Eighty-six percent found the proposed PBL and CBL well-structured. Ninety-five percent asserted the usefulness of additional teaching activities like tutorials and workshops for learning, expressing overall satisfaction with their organization. Every student affirmed enjoyment in active lessons with consistent student involvement, with approximately 70% favouring the Anatomage-enhanced-PBL approach, while others preferred the flipped classroom and CBL approaches. In addition, the percentage of students who said that the teacher stimulated/motivated their interest in studying anatomy has increased from 92.4% (n. 424; 2020, 2021, 2022 groups of the BSSM students) to 94.7% (n. 66; 2023 group). After self-assessment, surveys on anatomy knowledge demon-

strated positive outcomes, suggesting the effectiveness of this active learning method in enhancing students' understanding of anatomy.

Regarding the teacher-assessed efficacy of active learning versus traditional frontal didactic lectures, a comparative analysis of final marks from two different student cohorts revealed consistent methods and teacher involvement in exams across two consecutive years (2023 and 2024). The students exposed to multimodal active learning (n. 51, verbalized exams during first trimester of 2024) reached an average of final marks equal to 27.27/30 whereas the students exposed to didactic lectures reached 27.75 (n. 57, verbalized exams during first trimester of 2023; $p > 0.05$).

DISCUSSION

This study analyzes student assessments concerning the integration of traditional musculoskeletal and splanchnic anatomical lectures with an innovative multimodal-multidisciplinary learning approach. The adoption of new methodologies aims to foster critical thinking and active study, steering away from mere rote memorization of topics. Anatomists, recognizing the need for evolution in pedagogy, must explore inventive and stimulating multimodal strategies that encourage proactive and profound learning (Singh et al. 2019). The ultimate goal is to cultivate long-term memory in students, thereby enhancing engagement and aligning learning outcomes with their professional aspirations.

While traditional lectures remain the most widely employed and cost-effective means of teaching anatomy, their efficacy is marred by global criticism (Verma et al. 2024). Despite their capacity to impart substantial information swiftly, they often lead to disengagement and negative mental states such as frustration, anger, apathy, or somnolence. These detrimental states can be attributed to factors like audience dynamics, environmental conditions, and lecturer style (McLaughlin and Mandin 2001). It is crucial to acknowledge that, more often than not, the responsibility for these issues rests with the lecturers (McLaughlin and Mandin 2001). To prevent this and to plan effective lectures, the Association for Medical Education in Europe (Brown and Manogue 2001) and Italian ANVUR (Felisatti 2023) provided guidelines for lecturers and promoted students' active participation. Many different activities can be proposed during lectures to increase students' involvement (Giorgdze and Dgebuadze 2017). This study delves into the feedback garnered from undergraduate medical students, revealing a consistent inclination towards interactive teaching

methods over traditional lectures (Kuchynska et al. 2019, Keedy et al. 2011). The incorporation of interactivity into didactic lectures not only shifts the focus towards students but also heightens concentration and active participation. Interactive teaching methods allow encoding of information intertwined with emotional experiences, the emotional learning often leads to stronger and more enduring memories (Pare and Headley 2023, Wang et al. 2020, Tyng et al. 2017). The engagement of multiple brain regions involved in attention, perception, emotion processing, and memory consolidation contributes to the formation of strong and long term memories (Eriksson et al. 2015). However, the transition between traditional and active learning demands increased effort from educators, as the preparation of learning material and resources necessitates a more time-intensive approach (Kuchynska et al. 2019).

Recognizing the need for change, we adopted an interdisciplinary, hands-on, team-building approach based on Problem-Based Learning (PBL). PBL focuses on engaging students with curiosity, bringing future doctors closer to real-world medical contexts (Barrows 1980). PBL, introduced in the late 1960s at McMaster medical school, originated from the concern that students struggled to apply basic knowledge to clinical problems (Wijnia and Servant-Miklos 2019). Its inception by neurologist Howard Barrows, starting with real clinical problems, demonstrated increased skills in problem discussion and self-study among students (Tamblyn and Barrows 1980). This method, subsequently adopted by institutions like Harvard Medical School, transformed medical education, empowering students to become the protagonists of their learning journey (Trullas et al. 2022). PBL, following the Limburg University model with seven jumps/steps, encourages critical thinking, problem-solving, self-study, and teamwork (Schmidt 1983, Dangerfield, Bradley, and Gibbs 2000). It enables the application of theory to practice through real clinical cases, fostering a 'learn to learn' mindset. Moreover, PBL is an interdisciplinary method, emphasizing practical case studies with patient symptoms and diagnostic exams for analysis (Cheng et al. 2021). Beyond academic benefits, PBL promotes team building and effective collaboration (Ghani et al. 2021). In a PBL session, students share ideas without judgment, fostering an environment where cooperation is prioritized over evaluation. This collaborative experience contributes to building effective teamwork, helping students exchange information seamlessly as future doctors focused on preserving patient health.

In this study, six PBLs, centered around various medical conditions such as stroke, tumors, and diabe-

tes, were proposed to small groups of students. An innovative aspect was the integration of Anatomage table usage, offering a comprehensive view of anatomy related to the clinical cases presented. The Anatomage table not only enhanced the PBLs but also facilitated bonding among students during small group sessions. While cadaveric dissection remains a gold standard for anatomy learning (Burgess and Ramsey-Stewart 2015), this approach alone may fall short of meeting modern medical curricular needs. Integrating technological methods, such as virtual human cadaver dissection, offers a comprehensive educational model for anatomical science.

The study acknowledges certain limitations, including the online administration of post-session surveys and the voluntary nature of student participation, which may have biased responses selecting more motivated students from a single institute. Despite these constraints, the study underscores the value that students placed on PBL-based interactivity, indicating its potential incorporation into routine didactic teaching.

CONCLUSIONS

These findings constitute good evidence affirming the efficacy of Problem-Based Learning (PBL) as an augmentative approach capable of enhancing medical education of anatomy. By engaging successive generations of students in problem-centered learning, PBL fosters enthusiasm and proficiency, contributing significantly to the educational landscape.

In summary, this method serves as a compelling and practical avenue for medical students to promptly apply their acquired knowledge to patient care.

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Perceptions of Italian medical students on human dissection and modern technology in anatomy learning

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Abstract. Since 2021, the Azienda Ospedaliero-Universitaria of Sassari, Italy, has been authorized to preserve and utilize post-mortem tissues and bodies for research, study, and training. Before this date, no body dissection was performed. Medical students who wanted the opportunity were given the chance to go abroad for dissection courses. The primary purpose of the present study was to assess retrospectively, and using a questionnaire, the attitudes of medical students at the University of Sassari who had travelled to the University of Bordeaux to undertake anatomical body examinations. Students were invited to complete a survey, a 14-item questionnaire was developed. Over 85% of the students were very satisfied with the dissection course, the majority of medical students find the experience of dissection to be a unique and exciting opportunity, despite it being stressful and negative for some. Despite the wide range of electronic learning resources available today, unexpectedly with respect to our original hypothesis, the majority of our students have indicated that traditional dissection methods cannot be replaced by modern tools.

Keywords: medical students, perceptions, human dissection, anatomy learning.

INTRODUCTION

Human body dissection has been the main pedagogic approach for the teaching and learning of anatomy for more than 400 years (Persaud, 1984, 1997; Azer and Eizenberg, 2007; Moxham and Plaisant, 2014; Tubbs et al., 2019) and it is still often perceived by anatomists, medical students and the lay public as being essential for acquiring anatomical knowledge (Elizondo-Omaña et al., 2005; Patel and Moxham, 2006; Moxham and Moxham, 2007; Korf et al., 2008; Moxham et al., 2016). In Italy, however, there were no spe-

cific regulations for the donation of human bodies for anatomical examination (De Caro et al., 2009) until a legal decree was recently approved (Law-Decree n°10/20 dated February 10th, 2020, <http://www.senato.it/leg/18/BGT/Schede/Ddliter/50386.htm>). This law governs the criteria for body donation, including the requirement for informed consent from living donors, proper management of donors' bodies, and the identification of national reference centers (Maghin et al., 2020; De Caro et al., 2021; Orsini et al., 2021; Boscolo-Berto et al., 2023).

Since 2021, the Azienda Ospedaliero-Universitaria of Sassari, Italy, has been authorized to preserve and utilize post-mortem tissues and bodies for research, study, and training. Before this date, no body dissection was performed. Medical students who wanted the opportunity were given the chance to go abroad for dissection courses.

The primary purpose of the present study was to assess retrospectively, and using a questionnaire, the attitudes of medical students at the University of Sassari who had travelled to the University of Bordeaux to undertake anatomical body examinations. Our initial hypothesis was that the students were equally divided into those who see the educational and professional benefits of undertaking dissection and those who do not. Furthermore, given rapid technological developments resulting in the availability of an extensive range of electronic resources for anatomical education (Shaffer, 2004; McMenemy et al., 2014; Losco et al., 2017; Trelease, 2016), we evaluated the opinions of the students as to whether human dissection could, or should, be replaced by new technological 'tools. In this regard, since the students surveyed are often categorised as belonging to the Millennial generation (Benninger et al., 2014), our initial hypothesis was that the students believed that new technologies were preferable to human dissection. Understanding students' attitudes is important for fulfilling the major task of easing students' efforts and increasing students' engagement (McMenemy et al., 2018), for it is essential to understand what engages the new generation of learners before selecting a pedagogic approach. Students' preferences represent a useful tool when designing a course by helping educators identify effective teaching methods that are best suited to their students' learning styles (Davis et al., 2014).

2. MATERIALS AND METHODS

2.1. Educational context

Anatomy education at the Medical School of the University of Sassari, Italy, is organized into two annual

courses taught in the first and second years of a six-year medical curriculum.

In the first course (Anatomy I), students gain knowledge of general anatomical terms and locomotor systems. In the second course (Anatomy II) the curriculum consists of cardiovascular, respiratory, digestive, genitourinary and nervous systems as well as the lymphoid, endocrine and sense organs.

These courses are structured with traditional lectures and practical sessions. During the practical sessions, students have the opportunity to examine plastic models and view microscope glass slides to learn histology. All these activities are carried out with the support of teachers and near-peer tutors.

Dissections are only performed occasionally because the centre is new and most donors are still alive. We use only fresh materials, as we currently do not have any frozen bodies available.

2.2. Participants

Since 2013, medical students have been invited to participate in an extracurricular dissection course at the Anatomical Laboratory of Surgery School at the University of Bordeaux.

Usually, the course is scheduled at the end of the second year and lasts one week.

A maximum of fifteen students are admitted annually.

Students are chosen based on the highest score (28-30) achieved in the final examination of the anatomy course and on the general education curriculum. Students' involvement is voluntary.

After enrolling, students attend three meetings where a professional staff consisting of two anatomists and two plastic surgeons provide instructions on practical aspects such as the use of scalpels, forceps, and suture threads. They also explain dissection procedures and review the most important anatomical regions. The discussion also focused on the ethical behaviour to have in the dissecting room.

2.3. Dissection course

Throughout the dissection course, students were divided into two groups the, and one body was assigned to each group of seven or eight students. The same body was used throughout the course.

Within each group, students dissected the body in a rotatory manner under the supervision of the tutors. A sequence of regions to dissect was established before

starting and a checklist with the most important anatomical structures was projected on a screen during dissection. Tutors asked students to identify anatomical structures.

All students performed skin incisions and dissections based on anatomical planes.

The anatomical regions dissected were the neck, superior and inferior limbs (with a specific focus on some clinically relevant areas, i.e., cubital fossa, inguinal ligament, popliteal fossa, and femoral triangle), thorax (ventral and dorsal walls, organs of the thoracic cavity), and abdomen (ventral and dorsal walls, organs of the abdominal cavity). Each organ was further sectioned to view and appreciate its internal structure.

Participants were engaged for eight hours in day.

2.4. Data collection

A few months after the end of the dissection experience, students were invited to complete a survey. Invitations were sent by email to all participants. The email included a detailed description of the study along with a link to the questionnaire. All students were adequately informed about the study's purpose. To better guarantee anonymity and confidentiality regarding their data, we decided to not include the question about gender.

A 14-item questionnaire was developed by teaching staff: it comprised 1 item (Q1) to characterize the academic features of students, 12 items (Q2-Q13) to evaluate students' attitudes towards several aspects of the course (general organization, teaching modalities, teacher/student interaction, course's usefulness in improving anatomical knowledge, importance of dissection in clinical practice, possibility to replace dissection with modern technological tools) using a five-point Likert scale (1 poor, 5 excellent) and 1 item (Q14) to ask students in an open question format comments, criticisms, or suggestions regarding the dissection course.

The data were recorded in a database for statistical processing. Ethical approval was not required, as this was part of routine course evaluation.

2.5. Statistical analysis

An *ad hoc* electronic form was used to collect all study variables. Variables were described with absolute and relative (percentage) frequencies. In-between group comparisons of questionnaire items were performed with Chi-squared or Fisher exact tests when appropriate. A two-tailed *p*-value less than 0.05 was considered statistically significant. STATA version 16 (StataCorp, TX)

was the statistical package used to perform all statistical computations.

3. RESULTS

70 out of 95 students (73.6%) agreed to participate in this study.

The majority of students were in the second and third years of the medical curriculum (23, 32.9% and 24, 34.3%, respectively). The remaining were in the fourth (14, 20%), fifth (7, 10%), and sixth (2, 2.9%) years.

The majority of the students (87.1%, 61 out of 70) expressed high satisfaction with the course.

The participants' satisfaction was evaluated based on several factors: their overall satisfaction with the course (5 and 4 on the Likert scale: 46, 65.7% and 24, 34.3% respectively), the support provided by tutors (5 and 4 on the Likert scale: 63, 90.0% and 7, 10.0% respectively), and their level of engagement in the dissection activity (5 and 4 on the Likert scale: 60, 85.7% and 9, 12.9% respectively).

The majority of students reported an improvement in their anatomical knowledge after the dissection course, with 39 students (55.7%) rating it as a 5 on the Likert scale and 25 students (37.7%) rating it as a 4. Additionally, 77.1% of students found the course to be "very useful" (31 students, 44.3%) and "useful" (23 students, 32.9%) for developing their clinical skills.

70% of students considered dissection essential for medical training.

The majority of students (61.4%) believe that dissection cannot be replaced by digital learning tools, with 27.1% strongly agreeing and 34.3% somewhat agreeing. 21.4% of students are neutral on the issue, while 17.1% believe that dissection can be replaced, with 11.4% somewhat disagreeing and 5.7% strongly disagreeing.

All these results are shown in Table 1.

As illustrated in Table 2, there were no statistically significant differences between students of the second and third years.

Some students did not respond to the open-ended question. However, 50% of the participants shared their personal views on the dissection course. They appreciated the educational, emotional, and cultural value of this experience. The students highlighted the educational value, as they observed that they had solidified their anatomical knowledge through dissection. Additionally, they gained a better understanding of how structures are interrelated.

They encountered a cadaver for the first time, which is an important rite of passage for any future physician.

Table 1. Descriptive analysis.

Questionnaire	n (%)		Questionnaire	n (%)	
Which year of course are you enrolled in?	2	23 (32.9)	Is your anatomical knowledge improved after the stage? (Likert scale)	1	-
	3	24 (34.3)		2	-
	4	14 (20.0)		3	6 (8.6)
	5	7 (10.0)		4	25 (35.7)
	6	2 (2.9)		5	39 (55.7)
What is the level of your satisfaction for this stage? (Likert scale)	1	-	How much the stage's activities may have contributed to improve your clinical skills? (Likert scale)	1	-
	2	-		2	1 (1.4)
	3	-		3	15 (21.4)
	4	9 (12.9)		4	23 (32.9)
	5	61 (87.1)		5	31 (44.3)
What is the level of your satisfaction for the organizational aspects of the stage? (Likert scale)	1	-	How do you evaluate tutors' support during the stage? (Likert scale)	1	-
	2	-		2	-
	3	-		3	-
	4	24 (34.3)		4	7 (10.0)
	5	46 (65.7)		5	63 (90.0)
What is your assessment of the preparatory meetings for the stage? (Likert scale)	1	-	Do you think that dissection is essential in the training of future physician? (Likert scale)	1	-
	2	-		2	-
	3	6 (8.6)		3	5 (7.1)
	4	33 (47.1)		4	16 (22.9)
	5	31 (44.3)		5	49 (70.0)
Did you feel engaged in the stage's activities? (Likert scale)	1	-	Can be dissection replaced with digital tools? (Likert scale)	1	19 (27.1)
	2	-		2	24 (34.3)
	3	1 (1.4)		3	15 (21.4)
	4	9 (12.9)		4	8 (11.4)
	5	60 (85.7)		5	4 (5.7)
How do you evaluate your anatomical knowledge before the stage? (Likert scale)	1	-			
	2	2 (2.9)			
	3	24 (34.3)			
	4	29 (41.4)			
	5	15 (21.4)			

They described experiencing an unusual sensation and, based on this feeling, they dissected the human body with respect and an awareness of death. Lastly, the cultural value was related to the opportunity to get to know a university organized differently from the University of Sassari.

4. DISCUSSION

The field of anatomical sciences has experienced numerous changes over time. Despite these changes, dissection continues to be used as a teaching tool in many medical curricula. However, in some medical schools around the world, this practice has been reduced or replaced by other learning methods (Elizondo et al.,

2005; Flack and Nicholson, 2018). The primary aim of this study was to examine students' perceptions of a brief anatomy dissection experience.

In this study, over 85% of the students were very satisfied with the dissection course. One aspect they particularly appreciated was the high level of engagement during the course. The variables of engagement and motivation are of great importance with regard to the learning process. Active dissection engages all three domains of learning (cognitive, psychomotor, and affective) (Granger, 2004). Student engagement has been defined as students' involvement in activities that are likely to generate high-quality learning (Brown et al., 2018). Furthermore, student engagement is closely linked to motivation. Students with high motivation tend to be more engaged. The significance of motivation in learn-

Table 2. Descriptive analysis per year of study.

Questionnaire	Year of study						p-value
	2	3	4	5	6		
What is the level of your satisfaction for this stage? (Likert scale)	1	-	-	-	-	-	0.25
	2	-	-	-	-	-	
	3	-	-	-	-	-	
	4	1 (4.4)	5 (20.8)	1 (7.1)	2 (28.6)	0 (0.0)	
	5	22 (95.7)	19 (79.2)	13 (92.9)	5 (71.4)	2 (100)	
What is the level of your satisfaction for the organizational aspects of the stage? (Likert scale)	1	-	-	-	-	-	0.35
	2	-	-	-	-	-	
	3	-	-	-	-	-	
	4	10 (43.5)	9 (37.5)	2 (14.3)	3 (42.9)	0 (0.0)	
	5	13 (56.5)	15 (62.5)	12 (85.7)	4 (57.1)	2 (100)	
What is your assessment of the preparatory meetings for the stage? (Likert scale)	1	-	-	-	-	-	0.45
	2	-	-	-	-	-	
	3	2 (8.7)	1 (4.2)	2 (14.3)	1 (14.3)	0 (0.0)	
	4	11 (47.8)	10 (41.7)	9 (64.3)	3 (42.9)	0 (0.0)	
	5	10 (43.5)	13 (54.2)	3 (21.4)	3 (42.9)	2 (100)	
Did you feel engaged in the stage's activities? (Likert scale)	1	-	-	-	-	-	0.32
	2	-	-	-	-	-	
	3	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	0 (0.0)	
	4	1 (4.4)	5 (20.8)	1 (7.1)	2 (28.6)	0 (0.0)	
	5	22 (95.7)	18 (75.0)	13 (92.9)	5 (71.4)	2 (100)	
How do you evaluate your anatomical knowledge before the stage? (Likert scale)	1	-	-	-	-	-	0.27
	2	0 (0.0)	1 (4.2)	0 (0.0)	1 (14.3)	0 (0.0)	
	3	5 (21.7)	8 (33.3)	7 (50.0)	4 (57.1)	0 (0.0)	
	4	11 (47.8)	9 (37.5)	6 (42.9)	2 (28.6)	1 (50.0)	
	5	7 (30.4)	6 (25.0)	1 (7.1)	0 (0.0)	1 (50.0)	
Is your anatomical knowledge improved after the stage? (Likert scale)	1	-	-	-	-	-	0.37
	2	-	-	-	-	-	
	3	3 (13.0)	2 (8.3)	1 (7.1)	0 (0.0)	0 (0.0)	
	4	5 (21.7)	8 (33.3)	7 (50.0)	5 (71.4)	0 (0.0)	
	5	15 (65.2)	14 (58.3)	6 (42.9)	2 (28.6)	2 (100.0)	
How much the stage's activities may have contributed to improve your clinical skills? (Likert scale)	1	-	-	-	-	-	0.72
	2	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	0 (0.0)	
	3	5 (21.7)	4 (16.7)	3 (21.4)	3 (42.9)	0 (0.0)	
	4	8 (34.8)	6 (25.0)	7 (50.0)	1 (14.3)	1 (50.0)	
	5	10 (43.5)	13 (54.2)	4 (28.6)	3 (42.9)	1 (50.0)	
How do you evaluate tutors' support during the stage? (Likert scale)	1	-	-	-	-	-	0.40
	2	-	-	-	-	-	
	3	-	-	-	-	-	
	4	1 (4.4)	3 (12.5)	1 (7.1)	2 (28.6)	0 (0.0)	
	5	22 (95.7)	21 (87.5)	13 (92.9)	5 (71.4)	2 (100)	
Do you think that dissection is essential in the training of future physician? (Likert scale)	1	-	-	-	-	-	0.44
	2	-	-	-	-	-	
	3	1 (4.4)	1 (4.2)	3 (21.4)	0 (0.0)	0 (0.0)	
	4	4 (17.4)	5 (20.8)	4 (28.6)	3 (42.9)	0 (0.0)	
	5	18 (78.3)	18 (75.0)	7 (50.0)	4 (57.1)	2 (100)	

(Continued)

Table 2. (Continued).

Questionnaire	Year of study						p-value
	2	3	4	5	6		
Can be dissection replaced with digital tools? (Likert scale)	1	8 (34.8)	4 (16.7)	3 (21.4)	3 (42.9)	1 (50.0)	0.82
	2	8 (34.8)	9 (37.5)	4 (28.6)	3 (42.9)	0 (0.0)	
	3	3 (13.0)	6 (25.0)	4 (28.6)	1 (14.3)	1 (50.0)	
	4	3 (13.0)	2 (8.3)	3 (21.4)	0 (0.0)	0 (0.0)	
	5	1 (4.4)	3 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	

ing has been well established (Biggs, 1991), and research has shown that cadaveric dissection significantly impacts students' motivation (0; Shell et al., 2020). Although motivation was not quantified in this study, it is reasonable to assume that the dissection activity increased the motivation of our students.

They expressed how this experience made them more enthusiastic, not only because of what they saw (e.g., a three-dimensional view of the human body), but also because it was their first close encounter with death. Learning about human cadavers has aspects that are not easy to objectively evaluate, especially in relation to the approach to death (Winkelmann, 2007).

However, evidence suggests that dissection contributes to the development of humanistic and social qualities (Pizzimenti et al., 2016) and should be seen as a valuable opportunity that every future physician should experience (Pawlina et al., 2004).

The majority of medical students find the experience of dissection to be a unique and exciting opportunity, despite it being stressful and negative for some (Dinsmore et al., 2001). Our students also perceived the relevance of dissection, with most of them rating it as essential for their medical training. They agreed that dissection improved their anatomical knowledge and clinical skills.

The results are consistent with previous studies (Patel and Moxham, 2008; Kerby et al., 2011; Jayakumar et al., 2019; Gosh et al., 2017), which have shown that hands-on dissection is beneficial for students to enhance and solidify their knowledge gained from other teaching methods.

Despite the wide range of electronic learning resources available today, such as online websites and mobile apps, unexpectedly with respect to our original hypothesis, the majority of our students have indicated that traditional dissection methods cannot be replaced by modern tools. This finding is supported by other studies that reveal students' preferences for traditional methods over new ones (Biasutto, 2006; Ramsey-Stewart, 2010; Moxham and Moxham, 2007; Davis et al., 2014). However, even if the minority comprises 17.4%, we have to take into account the attitudes of some stu-

dents surveyed who were in favour of replacing dissection with other modern methods.

Similarly, other students or Authors have previously expressed their favour towards other tools, in particular prosection (McLaclan et al., 2004).

This finding shows that students have different learning styles, emphasizing the need to gather students' preferences to determine the best teaching approach for anatomy curriculum.

Some limitations of this study need to be addressed. Firstly, the number of participants was low and not every year of attendance was represented homogeneously; therefore, a larger sample size would enhance the power of this study. Additionally, this study was based on students' perceptions rather than outcomes; a future investigation based on students' performance will be conducted. Furthermore, this study evaluated students' perspectives on their dissection experience without comparing it to other teaching methods.

CONCLUSION

Student perceptions indicate a preference for body dissection in learning anatomy. Although digital tools facilitate students' approach to anatomical structures, the opportunity for direct contact with anatomical elements cannot be replaced.

Therefore, even though some medical schools have reduced or omitted dissection, an integrated approach that combines traditional and modern tools should be considered the best solution. Because no single tool fulfils curricular and individual requirements, educators should offer students the option of participating in dissections or learning through other methods.

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The role of innovation technology in teaching and learning strategies in anatomy curricula in dental hygiene school

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Abstract. *Purpose.* This research aims to assess the diversification of pedagogical and learning methodologies, leveraging advanced technological tools within a dental hygiene educational framework. *Methods.* Students enrolled in the dental hygiene program were considered as population sample, divided in two groups: The test group (N=16) subjected to the investigation of the virtual dissection table (VDT) and the control group (n=17) who attended lectures using traditional teaching method. The control group's performance was assessed through a 40-item multiple-choice questionnaire and an open-ended question; the test group was evaluated via a final test consisting of a presentation on an anatomical topic and a 40-item multiple-choice questionnaire. The final grade derived from the mean score of the final tests, and it was assigned on a scale of 30/30. Additionally, the test group's perceptions toward the use of the VDT were gauged through an evaluative questionnaire comprising 7 questions. *Results.* The study found a statistically significant difference in failure rates between the control group and the test group. However, the average exam scores did not show a statistically significant difference between the two groups, despite the test group showing some improvement. The evaluation survey results indicated high levels of satisfaction with the use of the VDT, with the quality of the virtual images, anatomical resources, and the user-friendly interface. Additionally, students strongly supported integrating traditional lectures with VDT laboratory sessions, with no negative feedback reported. *Conclusions.* The VDT represents an innovative anatomy teaching tool, warmly welcomed by healthcare profession students, whose performances were positively affected.

Keywords: applied anatomy, anatomy teaching, gross anatomy education, novel teaching modalities, undergraduate education, virtual anatomy.

INTRODUCTION

Human anatomy is that branch of the biomedical curricula of different schools in the field of biotechnologies and healthcare, concerning the study of the structure and organization of the human body, that involves the organs, tissues, cells and systems and how they interact (Turney, 2007).

Due to the importance of the knowledge of anatomy in laboratory and clinical procedures, it is mandatory to guarantee an effectiveness of anatomy learning (Bianchi et al., 2020; Goodwin, 2000). Professors and lecturers classically deliver their lessons using a digital presentation composed of captions, key words associated with the images which could reproduce a cadaver or a drawn of it (Meyur et al., 2011). Students have access to textbooks, diagrams, schemes, videos and atlas (Estai & Bunt, 2016). Due to the amount and complexity of anatomy subjects, students might apply a mnemonic learning method, resulting in low quality study of notions, and missing that information which are fundamental for clinical practice.

Commonly, human anatomy is included in the first years of curricula of medical, dental and healthcare professional schools. It can happen that the learning method, which differs from the one of high schools, is not well developed, with difficulties in acquiring permanently the important notions and information useful to progress in the academic and professional career (Iwanaga et al., 2021).

Other important factors which could affect the learning process in an academic environment are represented by the teaching time, increasing class size and increased cost of laboratory (Al Husaini et al., 2022).

For these reasons, the teaching and learning strategies represent a high-profile research topic and are currently being investigated by academic and pedagogic experts of the field.

Innovation technology is giving an aid to compensate for the lack of traditional teaching strategies. One of the most spread in the Western countries is the use of computer-based software providing a virtual cadaver and integrating notions and annotations (Moro et al., 2017). In addition, recently universities and institutions have been equipped with virtual dissection tables (VDTs) which provide and simulate the human anatomy dissection, histology and pathology, and clinical cases (Kavvadia et al., 2023).

All this material is useful in the undergraduate curricula and post-graduate, to diversify the learning strategies and refresh and review those notions that are used in clinical practices.

The students attending healthcare bachelor's degree have been reported in literature to face difficulties in the biomedical curricula, especially anatomy and physiology (Mitchell & Batty, 2009). The dental hygiene curriculum includes the study of gross anatomy at their first-year, and represent a sort of challenges for lectures and teachers to balance the gross anatomy notions, with the special area of head and neck, strongly appropriated to the type of this curricula (Kim & Kim, 2022).

In the attempt to fulfill the Sustainable Development Goal (SDG) number 4 proposed by the United Nations (UN), which aims to increase the quality of education (UN, 2015), the study aims to evaluate the teaching and learning strategies diversifications, relying on the modern technological instruments used in dental hygiene school.

MATERIALS AND METHODS.

Population

The population on which the use of the VDT was investigated consisted of students from the dental hygiene degree program, divided in two groups: the test group (N=16) undertook the blended method proposed, while the control group (n=17) attended traditional human anatomy classes.

Teaching method and exam evaluation used in the control group

The teaching approach used during anatomy lectures to the dental hygiene students included oral presentation of theoretical lectures; the total amount of the teaching classes was 30 hours of which 20 hours were dedicated to the traditional lectures and 10 hours consisted in laboratory practice on anatomical models. The curricula included the systematic anatomy topics (musculoskeletal system, cardiovascular system, respiratory system, digestive system, urogenital system, neuroendocrine system and stomatognathic system). The anatomy teaching approach tested was based on the combination of theoretical lectures given by the teacher with single sessions of two hours and a consequent one-hour-session of laboratory activities based on the study of the anatomy on traditional plastic models. The final evaluation consisted in a multiple-choice questionnaire of 40 questions composed of 5 choices of which only one answer was the correct one: no penalty was given if the one marked by the student was incorrect. In addition, an open-ended question about the stomatognathic system was part of the test. The final mark was obtained calculating the grade point average between the administered questionnaire and the open-ended question was given in a scale of 30/30.

Teaching method used and the final exam evaluation in the test group: the blended teaching approach

The traditional teaching approach used during anatomy lectures to the dental hygiene students included

oral presentation of theoretical lectures for an amount of 20 hours and 10 hours dedicated to the lectures using VDT (Anatamage© Table Convertible). The curricula included the systematic anatomy topics (musculoskeletal system, cardiovascular system, respiratory system, digestive system, urogenital system, neuroendocrine system and stomatognathic system). The anatomy teaching approach tested was based on the combination of theoretical lectures given by the teacher with single sessions of two hours and a consequent one-hour-session of laboratory activities based on the study of the anatomy on traditional plastic models and virtual dissection activities on VDTs (8 students per table), including a training on the use of the table and a hands-on session conducted by the students who were supervised by a teacher and a PhD student. The students had as final task to take screenshots of their own dissection for home-revision.

The used software of the VDT (Table EDU 8.0) is based on advanced imaging technology, which enables users to explore the human body and exploit interactive functionality, using the information and the images from the Visible Human Projects®. The reconstructions and the developed software, together with the touch screen hardware allows users to manipulate (dissecting, rotating, zooming) anatomical models in real-time, gaining a comprehensive view of the human body. The software also offers a library of histological specimens of human biological tissues, as well animated rendering describing the functions of the different systems such as the joints and the hearth rates.

The final exam in the test group consisted in a digital presentation made by each student about a single topic randomly assigned from the anatomy teaching program developed during the theoretical lessons and a multiple-choice questionnaire of 40 questions composed of 5 choices of which only one answer was the correct one: no penalty was given if the one marked by the student was incorrect. The final mark was obtained calculating the grade point average between the power point presentation and the administered questionnaire and was given in a scale of 30/30.

Outcomes: the opinions and the scores of the student

The investigation aimed to evaluate both the opinion of the students on the use of VDT and the efficacy in terms of exam success rate and scores.

As regards the opinion of the students, an evaluation survey on the use of the VDT was administered to all the students who gave consent to participate in the study; the students which did not give the consent, were excluded from the surveys. The evaluation questionnaire

Table 1. Evaluation questionnaire on the use of the VDT.

1. Did you already have experience using a digital anatomical visualization system?	· Yes · No
2. How satisfied are you with the quality of the images and anatomical resources provided by the virtual dissection table?	· Completely Satisfied · Very Satisfied · Satisfied · Nor Satisfied nor Unsatisfied · Unsatisfied
3. Have you encountered difficulty using specific features of the virtual dissection table? If yes, please specify in "Other"	· No · Yes · Other: _____
4. How useful do you think the study of anatomy using the virtual dissection table is for your subsequent clinical activity?	· Very Useful · Useful · Neutral · Useless · Very Useless
5. If you had the opportunity to improve the functionality of the virtual dissection table, what would you suggest?	_____
6. Did You enjoyed the presented anatomy lecture?	· Yes · NO
7. What would You suggest to improve the lecture?	_____

(Table 1) was administered at the end of the course, to all the compliant students. The survey was created using "Google online for Creator" on "Google workspace" and included seven questions administered in different types, thus five multiple choice questions and two open-ended questions. The Google Form was online, anonymous, and spread to the dental hygiene students using a link generated by Google form workspace.

The students were asked to evaluate their level of interest in the virtual dissection approach, their eventual experience with the same method proposed, the level of satisfaction about the lessons on VDT, the efficacy of its images, the grade of helpfulness of the software, and eventual proposals of improvement of the software itself and the way of developing of lessons on VDT.

Statistics

The parameters of the rate of failure and the mean values of the score were considered. Only the mean score of the students who successfully passed the final exam was compared between the two groups, who attended the lessons with the same teacher. The rate of failure and

the comparison between the two groups was evaluated using chi square tests on contingency tables. A result with a p value ≤ 0.05 was considered statistically significant. As regards the mean scores, unpaired t-student test was used to assess any significant differences, considering a p value ≤ 0.05 . The graphs and statistics were obtained using GraphPad Prism version 10.2.2 for Windows, GraphPad Software, Boston, Massachusetts USA, www.graphpad.com.

Ethics

The study was approved by the internal review board, with the reference number 41/2018, of which study project included this type of investigation on different curricula degrees.

According to the protocol of study approved by the internal review board, all the investigated students gave their consent before joining the study.

RESULTS

Dental hygiene students population

The number of students attending the test group of Dental Hygiene school was 16 and the number of students attending the control group was 17. All the students gave their consent to contribute to the study.

Evaluation survey

Overall, the answers to the survey were positive (Figure 1):16 students, even though without any previous experience with digital anatomical visualization, found easy to interact with the table and enjoyed the lectures. Half of the sample (n=8) found the blended method very useful for the clinical application and the other half (n=8) found the experience useful. As regards the quality of the images, most of the students was satisfied.

As regards the suggestions to improve the VDT, the majority (n=9) suggested to add Italian language (Table 2). As regard the suggestions to improve the teaching methods, only two comments were reported: increasing the hours in the laboratory and to integrate the use of plastic models (Table 2).

Exam scores

The number of students of the control group who failed the exam was 4. None of the 16 students who expe-

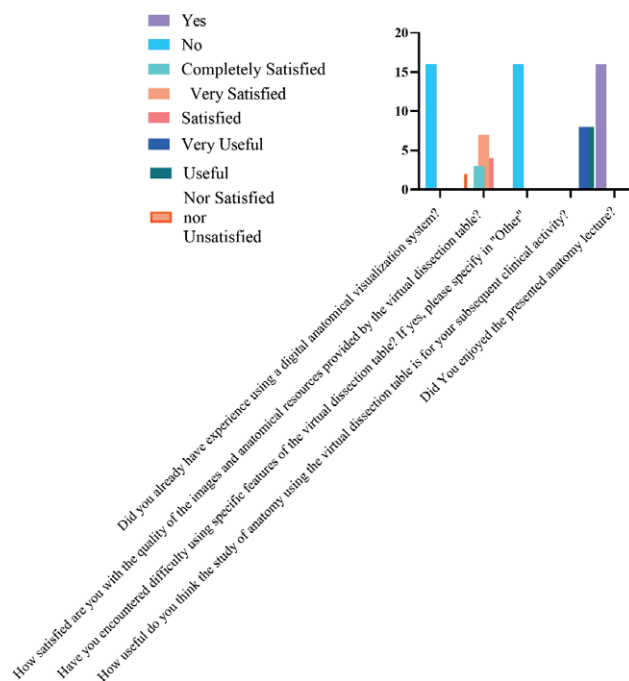


Figure 1. Graphical representation of the survey results. Graph obtained using GraphPad Prism version 10.2.2 for Windows, GraphPad Software, Boston, Massachusetts USA, www.graphpad.com.

Table 2. Most notable answers from the students' comments.

Question	Notable Comments
If you had the opportunity to improve the functionality of the virtual dissection table, what would you suggest?	Add Italian Language Add More Language
What would You suggest to improve the lecture?	Increase the laboratory hours Continue to use both VDT and Plastic Models

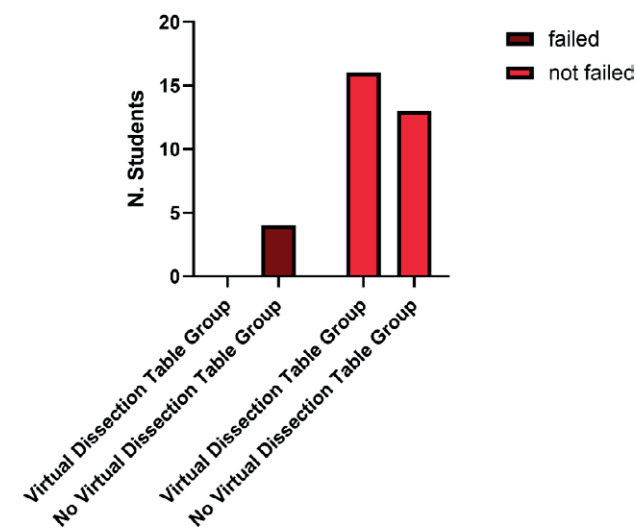
rienced and integrated the VDT teaching and learning strategies failed the exam. The chi square test on contingency table resulted statistically significant (Figure 2)

The quality of the test group exam in terms of scores was better than the control group, but not statistically significant (Figure 3).

DISCUSSION

The blended teaching method was effective on students' performances

The core of the anatomy curricula in the undergraduate courses aims to provide the right and neces-

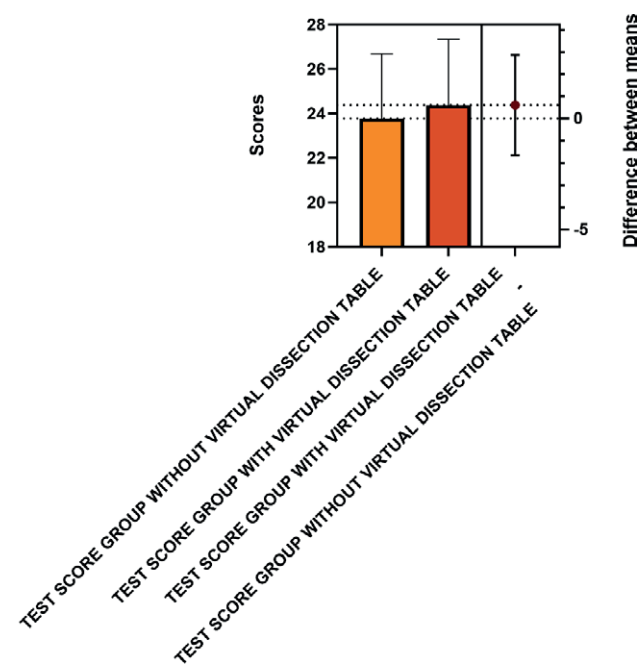


	failed	not failed
Virtual Dissection Table Group	0	16
No Virtual Dissection Table Group	4	13

P value and statistical significance	
Test	Chi-square
Chi-square, df	4.284, 1
z	2.070
P value	0.0385

Figure 2. Separate graph bar showing the differences between the students who attended the blended teaching method using the virtual dissection table and the control group. The table inset reports the contingency table and the related Chi Square test. P value is < 0.05, showing the difference is statistically significant.

sary knowledge of human body and oral cavity features for clinical application. The VDT blended method has showed a significant adjuvant role in the anatomy education, when combined with the traditional teaching methods, represented by topographical anatomy textbooks and cadaveric dissection sessions, representing a new blended-learning approaches as Chytas et al. investigated conducting a general review on this fundamental topic in 2023 (Chytas et al., 2023). The proposed blended teaching method, represented by the combination of traditional lectures and innovative laboratory activities conducted on VDT resulted effective in students' academic performances. The difference in terms of failure rate between the control group, composed of 17 students who did not attend to VDT activities, and the test group of 16 students who experienced the blended teaching method, was statistically significant. However, the differences between the two classes in term of mean of the exam scores, even with an improvement in the test group, were not statistically significant. The efficacy of using VDT as alternative method of teaching human anatomy was showed by different studies: in the study of Patniak et al., the authors



Unpaired t test	
P value	0.5862
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.5510, df=27

How big is the difference?	
Mean of column A	23.77
Mean of column B	24.38
Difference between means (B - A) ± SEM	0.6058 ± 1.099
95% confidence interval	-1.650 to 2.862
R squared (eta squared)	0.01112

Figure 3. Estimation plot showing the differences between the means of the scores assigned to the students who attended the blended teaching method using the virtual dissection table and to the control group. The table inset reports the Unpaired t test, the mean of the scores, the 95% confidence interval and the related Chi Square test. P value is > 0.05, showing the difference is not statistically significant.

evaluated the effectiveness of Anatomage© virtual dissection as a teaching tool in comparison with traditional dissection in Neuroanatomy curriculum for 3rd year Physiotherapy students, showing that test scores in the group of students who were taught using the VDT were better than the group of students taught using the traditional cadaveric method (Patnaik et al., 2024). In the study conducted by Rosario et al., VDT was investigated as a supplemental learning method, similar to the blended method proposed by the current study. However, the study investigated the traditional dissection method combined with the use of VDT in the study of Head and Neck Anatomy, showing that VDT implemented the learning flow of the students (Rosario, 2022).

The positive opinions of the students

The results of the evaluation survey based on the level of satisfaction on the use of VDT demonstrated positive perceptions of this innovative teaching and learning instrument. Indeed, the majority of the students was well satisfied with the use of the virtual dissection table which was never experimented, highlighting the satisfaction with the quality of the provided virtual images and the anatomic resources. Furthermore, the interface of the VDT appeared user-friendly to the whole test group of students who had no issues in interacting with it.

About the usefulness of integrating traditional lectures with laboratory on virtual dissection table, the evaluation survey showed a very positive results from students' opinions, without any negative feedback, showing the effectiveness of using VDT as demonstrated by different authors: in the study of Alasmari et al., authors administered to medical students an electronic questionnaire composed of 6 questions regarding the effect of using a 3D VDT (Anatmage®), combined with cadaveric dissection activities, to 78 medical students. The majority reported a great level of satisfaction in using VDT, thanks to the imaging facility available on the table, which was useful to improve their knowledge in human anatomy (Alasmari, 2021).

In another study conducted by Ralte et al., authors investigated the blended learning method in first year of Bachelor of Medicine and Bachelor of Surgery (MBBS) students through a semi-structured questionnaires whose results confirmed that the use of VDT (Sectra®) followed by cadaveric dissection was preferred as a teaching method by the 60% of the students (Ralte et al., 2023).

Similar studies have investigated the adjuvant role of VDT when combined with the traditional teaching and cadaveric dissection methods using both two parameters of investigation, thus the rate score resulted from the final exam following to the academic curriculums and an evaluation questionnaire administered to the students: in particular, in the study of Malhotra et al., a comparative study was conducted in order to assess the eventual effectiveness of VDT in comparison with the cadaver dissection laboratories, demonstrating that students achieved more than 50% marks thanks to the blended method; however, the evaluation questionnaire revealed a particular data about the role of VDT, demonstrating that student appreciated the virtual dissection study as a complementary method associated to the cadaveric dissection which still remains fundamental and not replaceable from the VDT (Malhotra et al., 2016).

The positive outcome of using VDT as supplemental reaching method was also demonstrated by Deng et al. in 2018 who assigned 120 medical students into 4 classes divided in two groups: the test group was represented by two classes who attended blended teaching sessions composed of traditional methods and digital virtual simulation (DVS) method, while the control group was assigned to the traditional methods used alone; the result of the final exams showed a statistically significant difference between the two groups, revealing an higher mean score achieved from the test group than the control group. At the same time, students demonstrated their approval of DVS as adjuvant teaching method (Deng et al., 2018). Furthermore, a recent study conducted by Emadzadeh et al. in 2023 confirmed the potential for virtual dissection to increase anatomical education: their investigation consisted in evaluating the performance of second-year undergraduate medical students after studying gross anatomy by VDT, representing the test group, or topographical anatomy textbooks as control group. The final score and the evaluation survey following the completion of the anatomy curriculum showed a significant gain in results and satisfaction about the tested teaching method, when compared to the traditional one (Emadzadeh et al., 2023).

Finally, the survey administered in the current study specifically asked students to propose eventual improvements of the software Table EDU 8.0. Most of the students, speaking mainly Italian language, proposed to implement the software with their mother tongue language, while some students proposed to increase the number of teaching hours on virtual dissection table combined with the direct manipulation of plastic models. However, most of the students showed that there was not the necessity of improving or changing the actual blended method proposed.

Strengths, limitations and future perspectives

The current study showed how the use of innovative technology lead the students to an enthusiastic learning approach and environment. However, the small sample size represents a strong limitation. Exploiting the new instruments which academics have in place is fundamental to improve the quality of teaching methods, and, as consequence, the learning flow of students. The need of allowing the students to learn in the most effective way, and more practically, an eventual another pandemic, such as the COVID 19 one, motivate governments and institutions to invest in the technology (Varvara et al., 2021). The current development of the augmented reality system represents the future which paves the way

for the study of human body thanks to the new tools and the possibility of perceiving the anatomical structure through innovative visual and haptic instruments such as haptic gloves and virtual reality glasses (Bisht et al., 2019).

Indeed, the manipulation moments during hands-on sessions, being on cadaver or models, is crucial in the medical and healthcare education (Varvara et al., 2021). As reported by Sajdłowski study on education online due to COVID19 pandemic, the hands-on and practical training sessions represent unique moments, unreplaceable by e-learning or only-digital session (Sajdłowski et al., 2021).

On the other hand, another challenge is represented by the integration of the virtual reality (VR), augmented reality (AR) and mixed reality (MR) which are involved in the application of metaverse to enhance learning and teaching of human anatomy (Iwanaga et al., 2023).

CONCLUSIONS

Anatomy course is always reminded by medical, dental, and healthcare former students as the first difficult exam in their curricula. Innovation technology, when integrated for the diversification of the teaching strategies, allows students to improve their learning strategy, keeps in their mind the memory of the anatomy course as a positive experience, and increase their interests in the topic.

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A comparative quali-quantitative analysis of student perspectives on microscopic anatomy labs: traditional glass slide versus virtual slides approach

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Abstract. This study, with its potential to significantly impact the field of medical education, is a testament to the active participation and invaluable contributions of a cohort of 59 first-year medical students. These students, the future of medical practice, shared their perspectives on two distinct methods of learning microscopic anatomy—traditional glass slide and microscope-based lessons versus online microscopical anatomy lessons employing the virtual slides in the Histology Guide website. They attended traditional microscopic anatomy lessons using a histology glass slide and a light microscope; the same group attended online lessons using virtual slides. Their feedback was gathered through a comprehensive questionnaire of 27 questions, which assessed effectiveness, convenience, engagement, and overall preference. Our quantitative and qualitative results clearly show that the same students who attended both the in-person and distance microscopic anatomy labs, while appreciating the usefulness and effectiveness of the two types of experiences, significantly prefer the in-person microscopic anatomy labs, judging the latter to be more interactive, due to the possibility of being able to directly use an optical microscope and slides containing histological preparations and the opportunity to work in groups with other students, being able to interact directly with the lecturer in the classroom. The remote experience of the light microscopy lab also allowed them to access it at their preferred times and review the lab several times during their available time. As reflected in the findings, these students' preferences and perceptions regarding these contrasting educational modalities offer insights crucial for refining anatomy teaching practices in medical education.

Keywords: microscopy, virtual microscopy, microanatomy, medical education, technology-enhanced instruction.

INTRODUCTION

Understanding medical students' preferences between distance learning and face-to-face teaching, particularly in the context of the COVID-19 pandemic, is a topic of significant interest. Our study, which stands out for its novel and explicit comparison of the traditional glass slide and microscope-based lessons with online microscopical anatomy lessons employing the virtual slides on the Histology Guide website, builds on the valuable insights provided by numerous studies in this area. For instance, Khalil et al. (2020) examined undergraduate medical students' perceptions of synchronized online learning during the pandemic, revealing a shift to online methods (Khalil et al., 2020). Similarly, Abbasi et al. (2020) highlighted students' perceptions of e-learning during COVID-19, indicating a transition to online platforms (Abbasi et al., 2020). However, Rahm et al. (2021) noted that despite the necessity of e-learning due to the pandemic, medical students initially preferred face-to-face teaching in clinical settings (Rahm et al., 2021).

Similarly, medical students' preferences for microscopic anatomy labs have been studied, particularly in the context of the COVID-19 pandemic. Studies have explored students' perceptions of online versus traditional face-to-face teaching methods for anatomy education. Singal et al. (2020) found that most students missed traditional anatomy learning, including face-to-face lectures and mentor interaction. Similarly, Mahdy & Sayed (2022) reported that while a significant percentage of students were satisfied with online learning materials for anatomy, there was still a preference for face-to-face teaching. This sentiment was echoed by (Mahdy & Ewaida, 2022), who highlighted that students missed various aspects of anatomy education, including face-to-face lectures and interaction with mentors.

Practical lessons in microscopic anatomy can classically be conducted either in-presence within the microscopic anatomy laboratories, through traditional microscopic anatomy teaching methods, using classical light microscopes and histological preparations on slides that are observed and discussed together with students, or through online microscopic anatomy learning platforms, where students are at a distance and use their computers to observe histological preparations, always guided by the lecturer who is remotely located (Hortsch et al., 2023A, B; Meyer, 2023).

Also related to technology's increased use and low cost, virtual microscopy is increasingly replacing the traditional use of microscopes and histological slides in microscopic anatomy laboratories, with both advantages and disadvantages to students (Hortsch et al.,

2023A). The use of laboratories equipped with optical microscopes and adequate collections of histological preparations may be costly for those universities where these resources are not possessed. At the same time, the increase in the number of students attending Italian medicine and surgery course degrees requires, in many cases, a sharp rise in rotations within the available laboratories due to the small number of faculty members available for this type of practical activity. The use of technology, in these cases, can be of great help to properly carry out this practical part of the study of microscopic anatomy. However, it must always be able to lead to the self-directed and independent learning that students need (Meyer, 2023).

In this study, our primary objective was to analyze the perceptions of the students who, in conducting the course on the microscopic anatomy of the respiratory, digestive, and urogenital systems, have experienced both types of hands-on laboratories in the presence and at a distance. We aimed to understand their preferences, engagement levels, and overall satisfaction with these contrasting educational modalities.

MATERIALS AND METHODS

The course of the human anatomy module 2

Module 2 of the human anatomy course of the master's degree program in medicine and surgery in the Faculty of Medicine and Psychology at the Sapienza University of Rome covered the study of the macroscopic and microscopic anatomy of the lymphoid system, respiratory system, digestive system, urogenital system, male reproductive system, and female reproductive system. This teaching module was held in the first year, second teaching semester, from March to May of the academic year 2022-2023. Students enrolled (n=220) who attended at least 67% of the mandatory Anatomy Module 2 course were eligible for an ongoing examination with oral and practical tests (autopsy identification of the organs, microscopic examination, and diagnosis of the structure of the organs).

Students took, in addition to the theoretical lectures given in the classroom, N. 2 macroscopic anatomy labs with the cadaver using the prosection, N. 4 macroscopic anatomy labs using the Sectra® 3D anatomical table, and the following hands-on microscopic anatomy lectures (delivered both in-person and remotely):

A) four practical laboratories on microscopic anatomy conducted in the presence at the laboratories of the Department of Anatomical Histological, Medical-Legal, and Locomotor Sciences, in the presence of the lecturer

who showed histological preparations using an optical microscope equipped with a camera connected to monitors on the tables where each student had a slide similar to the one shown by the lecturer and an optical microscope that they used. Practical laboratories included the study of microscopical anatomy of the following organs: 1) the trachea and lungs, 2) the esophagus, stomach, and duodenum, 3) the mesenteric small intestine and large intestine, and 4) the lymph node and spleen.

B) four practical laboratories on microscopic anatomy delivered remotely using computers and the Histology Guide website (Sorenson and Brelje, 2014). In this case, the lecturer showed the specimens by sharing their screen with the remotely connected students. The lecture, delivered through the Google platform of Sapienza University of Rome, was recorded and saved in a drive shared with the students who could independently see the lecturer's explanation. Later, the same students could log on to the site and independently view the preparations for the desired time. It should be pointed out that the platform allows dynamic viewing of the entire histological preparation, moving the field and varying the magnification used. The four hands-on distance learning lectures included the study of microscopical anatomy of the following organs 1) the liver and pancreas; 2) the kidney and urinary bladder; 3) the uterine tube, uterus, and ovary; and 4) the testis, epididymis, and prostate.

Student sampling

Students enrolled in the first year of the master's degree program in medicine and surgery in the Faculty of Medicine and Psychology at the Sapienza University of Rome were enrolled in the study after taking the entire Human and Clinical Anatomy module 2 for at least 67% of the mandatory anatomy module 2 course. The students asked to complete the evaluation questionnaire were selected from those who had attended at least three in-person and at least three distance workshops. The selection was conducted randomly, using simple random sampling. There were 56 students enrolled in completing the questionnaire (n=56; n=39 female and n=17 male, mean age SD = 19.91.02).

Students' views

The questionnaire used in this study, validated by Familiari et al., 2013, was administered after the last microscopic anatomy course laboratory lesson to all the students who had attended at least three of the four microscopic anatomy labs either remotely or in their

presence. The students were asked to fill out the questionnaire anonymously. Informed consent to participate was obtained from each student after the aim and purpose of the study had been thoroughly explained, ensuring the validity and reliability of the data collected.

The questionnaire consisted of three subsections, A-C. Subsection A was devoted to evaluating the virtual microscopy laboratory, subsection B was dedicated to assessing the in-person microscopy laboratory, and subsection C consisted of dichotomous items regarding the reasons behind their preferences. More than one answer to the questions proposed in subsection C of the questionnaire was possible. Subsections A and B contained nine items related to the laboratory types, distance, and presence, respectively. Students responded to each item using a 5-point Likert scale (1=strongly disagree, 2=disagree, 3=neither agree nor disagree, 4=agree, 5 = strongly agree).

Subsection C contained descriptive items mainly dealing with the reasons that had determined students' preferences between distance and in-person microscopic anatomy practical laboratories.

Data analysis of students' views

Individual responses obtained using the Likert scale were treated as variables measured at equivalent intervals and then means and standard deviation were computed as adequate statistics for this measurement level (Cario and Perla, 2008; Finney & Di Stefano, 2013). Pairwise comparisons of sections A and B were performed using the t-Student test. Statistical significance was established at $p \leq 0.05$. The size effect was calculated using the Cohen's-d test. The general guidelines for interpreting the effect size are as follows: 0.2 = small effect; 0.5 = moderate effect; 0.8 = large effect (Lakens, 2013).

Cronbach's Alpha coefficient assessed the internal consistency of items from sections A and B. A Cronbach's Alpha value higher than 0.70 is adequate for the questionnaire's internal consistency (Bland and Altman, 1997). The data were analyzed using IBM-SPSS 27 (<https://www.ibm.com/it-it/analytics/academic-statistics-software>).

RESULTS

Questionnaire Sections A and B

As shown in Table 1, the answers showed that a very high number of students expressed their appreciation for both types of courses, online and in-person. In both cases, the mean scores were far higher than the "theoretical" mean of 3.

Table 1. Student answers are given as mean and standard deviation to questions in sections A and B of the questionnaire.

Questions	Mean	SD
A1 How much did you enjoy the virtual microscopy lab experience?	4,36	0,724
A2 How helpful was the virtual microscopy lab experience in understanding microscopic anatomy?	4,07	0,71
A3 How engaging was the virtual microscopy lab experience?	3,57	0,499
A4 To what extent did the virtual microscopy lab experience meet your learning needs?	3,79	0,948
A5 How likely will you recommend the virtual microscopy lab experience to other students?	4,57	0,599
A6 How comfortable were you with the technology used in the virtual microscopy lab experience?	4,34	0,815
A7 How clear were the instructions provided for the virtual microscopy lab experience?	4,29	0,706
A8 How sharp were the digital images for the virtual microscopy lab experience?	4,43	0,628
A9 How satisfied were you with the virtual microscopy lab experience overall?	4,57	0,628
B1 How much did you enjoy the in-presence microscopy lab experience?	4,71	0,456
B2 How helpful was the in-presence microscopy lab experience in understanding microscopic anatomy?	4,29	0,594
B3 How engaging was the in-person microscopy lab experience?	4,32	0,716
B4 To what extent did the in-presence microscopy lab experience meet your learning needs?	4,07	0,806
B5 How likely will you recommend the in-presence microscopy lab experience to other students?	4,64	0,483
B6 How likely will you recommend the in-presence microscopy lab experience to other students?	4,36	0,483
B7 How clear were the instructions provided for the in-presence microscopy lab experience?	4,23	0,539
B8 How sharp were the images seen with the microscope for the in-presence microscopy lab experience?	4	1,079
B9 How satisfied were you with the in-presence microscopy lab experience overall?	4,68	0,606

We compared the items related to the same aspect of the course using a t-test for paired samples. The following table (Table 2) presents the results of this analysis. As can be easily seen, except for Items 6 and 7, all the comparisons were statistically significant, evidencing a higher appreciation for the “in presence” laboratory. Cohen’s d indices of effect size evidenced moderate to large effect size for the statistically significant effects, except for items 5, 7, and 9, whose effect sizes were small.

To obtain a summary score of appreciation of Online and Presence courses, we aggregated the scores across, respectively, the nine items related to these courses. Aggregating these scores is legitimate by the very high Cronbach alphas (being .98 and .95, respectively, for the online and the in-presence laboratory). The mean average scores for the online and in-presence labs were 4.21 (SD = .65) and 4.38 (SD =.57). These aggregated scores confirm the strong appreciation of the two courses. The mean difference between the scores was -.162 resulting statistically significant, $t(55) = -8.128$, $p > .001$, $d = -1.086$.

Questionnaire Section C

The questions in section C of the questionnaire were partly dichotomous and devoted to highlighting the motivations behind the students’ preferences in the study. On the first question about the preferred over-

Table 2. Results of statistical analysis between the responses of sections A and B of the questionnaire.

	Mean Difference	T	P	Cohen’s d
A1 vs. B1	-0,357	-5,528	<,001	-0,739
A2 vs. B2	-0,214	-3,873	<,001	-0,518
A3 vs. B3	-0,75	-12,845	<,001	-1,717
A4 vs. B4	-0,286	-4,69	<,001	-0,627
A5 vs. B5	-0,071	-2,057	0,022	-0,275
A6 vs. B6	-0,018	-0,207	0,418	-0,028
A7 vs. B7	0,054	0,83	0,205	0,111
A8 vs. B8	0,429	5,104	<,001	0,682
A9 vs. B9	-0,107	-2,569	0,006	-0,343

all experience, the virtual microscopy lab received no response; 14.3% of the students stated that they had no particular auto preference, while 85.7% indicated that they preferred the in-person lab experience (Fig. 1).

The second question was devoted to indicating what the student had liked about the in-person lab experience. The student could select more than one of the four response options. 100% of the respondents indicated that they appreciated having a hands-on experience with the light microscope; 85.7% of the students stated that they enjoyed the very interactive experience; 75.4% of the respondents indicated that they appreciated being able to see slides with histological preparations in person;

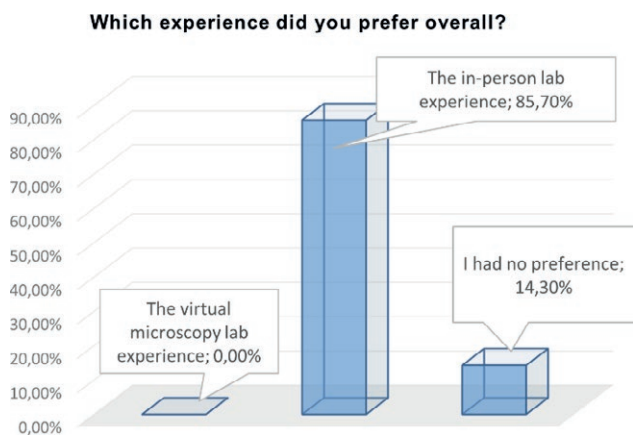


Figure 1. Students’ opinion about the preferred overall experience.

and 33.3% stated that they enjoyed being able to work in groups with other students (Fig. 2A).

On the other hand, the third question was devoted to exploring what the student did not enjoy from the in-person laboratory experience. The student could select more than one of the four response options. None of the student respondents (0.0%) highlighted difficulties in using the light microscope or handling glass slides; 35.7% of the students indicated less flexibility in terms of schedules; 14.3% of the students showed the need to be physically in the lab, while only 7.2% indicated, under “other,” difficulty in getting to the location (Fig. 2B).

The fourth question indicated what the student had enjoyed about the virtual microscopic anatomy lab experience. Again, the student could select more than one of the four response options. 71.4% of the students surveyed indicated that they liked the ability to access the

lab experience remotely; 64.3% of the students stated that they preferred the ability to review the lab experience at their own pace, while 35.7% indicated that they preferred the ability to zoom in and out of images. 7.5% of students indicated, under “other,” explaining all histological structures examined in detail (Fig.3A).

On the other hand, the fifth question was devoted to exploring what the student did not enjoy from the distance laboratory experience. The student could select more than one of the four response options. None of the students surveyed (0.0%) indicated difficulty using the technology, while 72.6% indicated less interactivity with other students or the lecturer; only 21.4% stated a limited ability to ask questions in real-time. Some students (14.3%) indicated under “other” that they did not like the proposed schedules, suboptimal audio quality, and problems with the remote connection (Fig. 3B).

In the sixth question, students were asked which laboratory experience, remote or in-person, they perceived most helpful in understanding microscopic anatomy. 57.2% of students indicated that both experiences had been equally beneficial. 35.7% stated the in-presence laboratory experience as more functional, while only 7.3% indicated the virtual microscopy laboratory experience as more practical. No students (0.0%) showed that the two experiences were perceived to be of little use (Fig. 4).

The last three questions in section C were devoted to the specificity of the content compared to the classroom lecture.

In the seventh question, students were asked whether the in-person laboratory experience provided content different from the classroom anatomy microscopy lecture. 57.1% of students responded that in these in-person labs, they had covered some of the same content as the

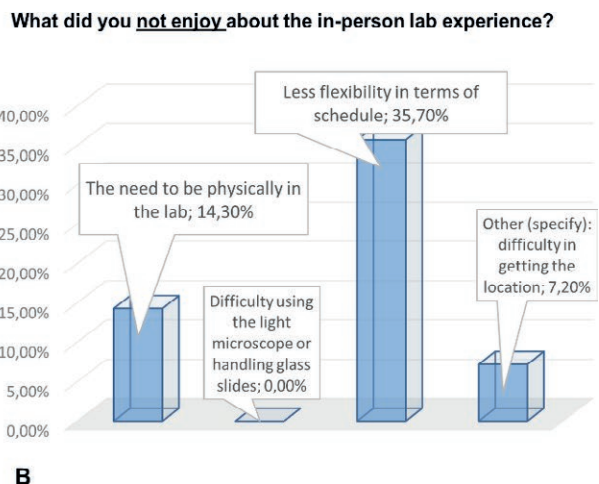
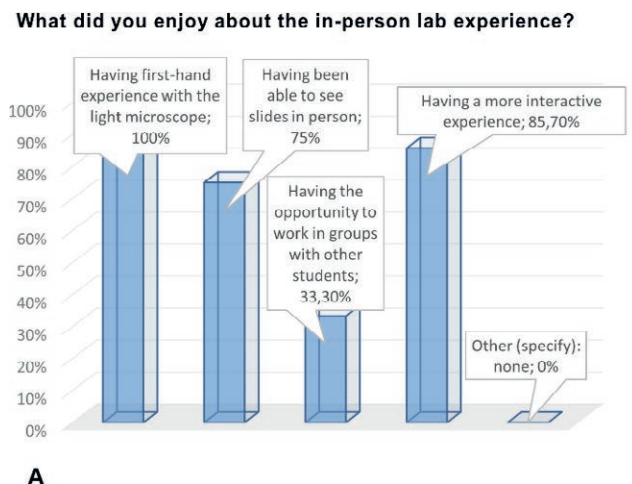


Figure 2. Students’ opinion about the in-person lab experience.

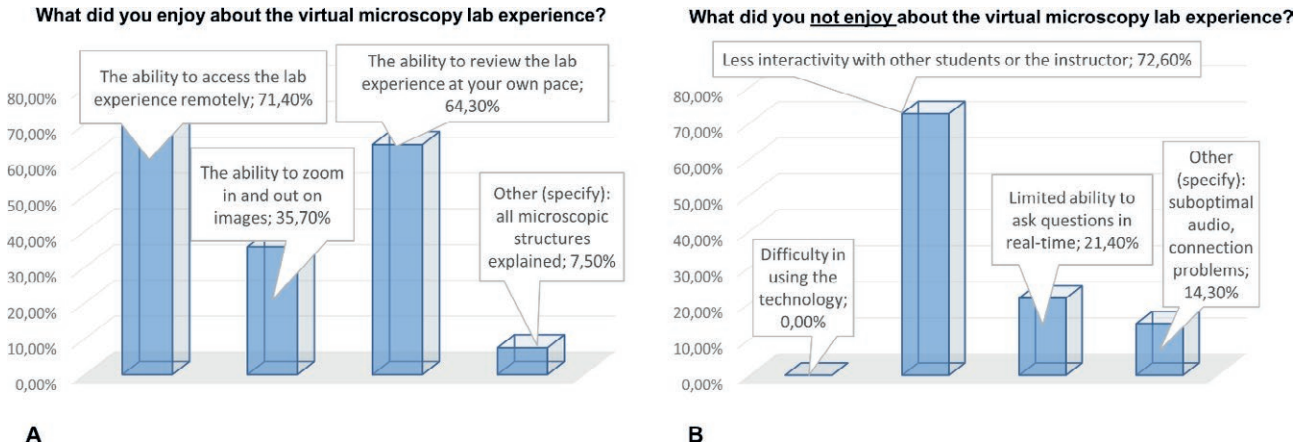


Figure 3. Students' opinion about the virtual microscopy lab experience.

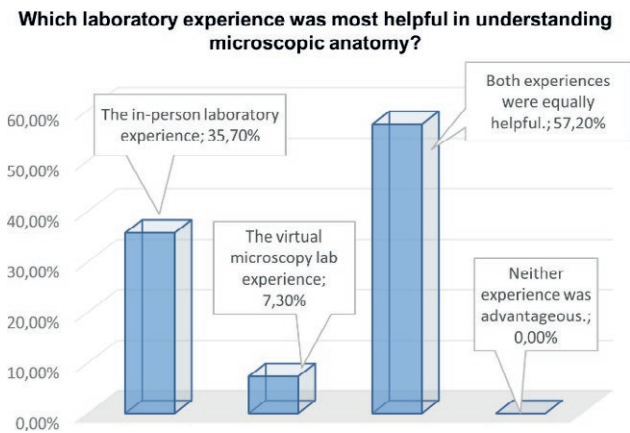


Figure 4. Students' opinions about the most helpful lab experience.

theoretical lectures but in a different way and with a different emphasis. 28.6% responded that the in-person labs had covered some additional and more detailed content than the classroom lecture. At the same time, only 14.3 percent of students thought the in-person labs covered the same topics as the classroom course, with no particular differences (Fig. 5A).

Similar results were obtained in the responses to the eighth question, in which students were asked whether the virtual laboratory experience provided teaching content different from the regular lecture on microscopic anatomy. In fact, in this case, 49.7% of students answered that the virtual laboratory had covered some of the same content as the theoretical lectures but in

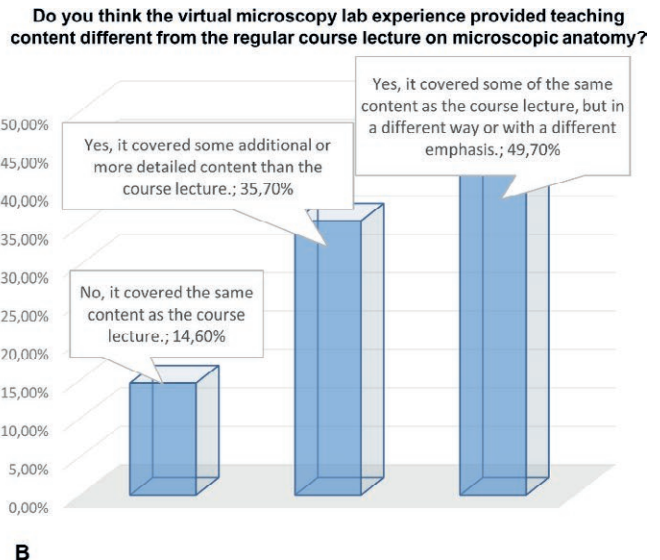
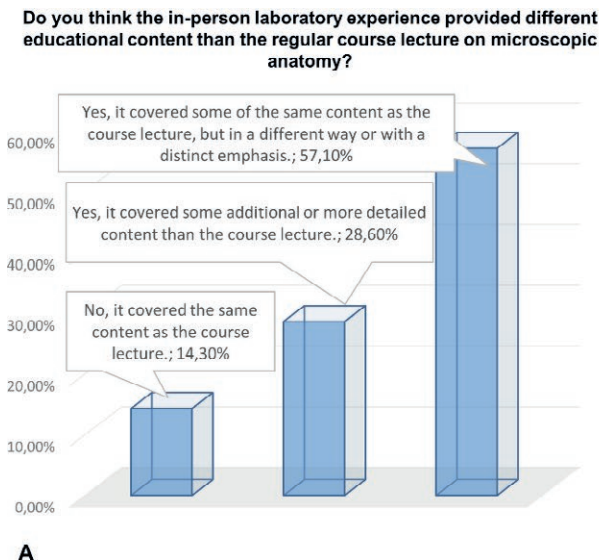


Figure 5. Students' opinions about the educational content of the two lab experiences.

Which laboratory experience provided different educational content than the usual lecture on microscopic anatomy?

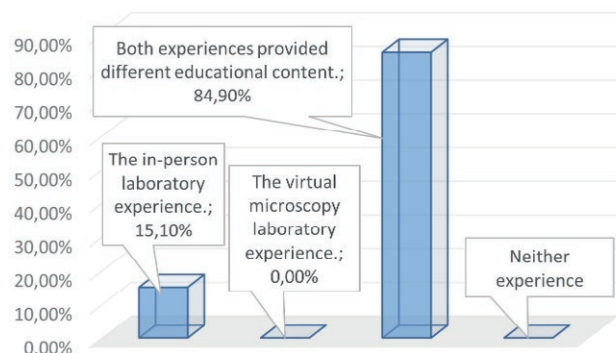


Figure 6. Students' opinions about different educational content between labs and lectures.

a different way and with a different emphasis. 35.7% responded that the virtual labs had covered some additional or more detailed content than the theoretical lectures. At the same time, only 14.6% of students indicated that the virtual labs had covered the same content as the theoretical lectures in the course (Fig. 5B).

The last question, the ninth, directly compared the two experiences. Students were asked which laboratory experience had provided different educational content than the usual classroom lectures on microscopic anatomy. In this case, 84.9% of the students responded that both experiences had provided different educational content; only 15.1% identified the in-person laboratory experience; no student (0.0%) indicated the virtual microscopy laboratory experience. No students (0.0%) indicated that none of their experiences had provided different educational content (Fig. 6).

DISCUSSION

Our quantitative and qualitative results clearly show that the same students who attended both the in-person and distance microscopic anatomy labs, while appreciating the usefulness and effectiveness of the two types of experiences, significantly prefer the in-person microscopic anatomy labs, judging the latter to be more interactive, due to the possibility of being able to directly use an optical microscope and slides containing histological preparations and the opportunity to work in groups with other students, being able to interact directly with the lecturer in the classroom.

The remote experience of the light microscopy lab also allowed them to access it at their preferred times and review the lab several times during their available time.

The teaching methods delivered to students regarding the curricular structure of microscopic anatomy teaching, microanatomy didactics and laboratory, microscopy laboratory format, and other shared learning resources are similar to those of universities worldwide (Hortsch et al., 2023A). The site used for our remote microscopic anatomy laboratories, "Histology Guide" (Sorensen and Brejle, 2014), also appears to be on the list of open, freely accessible websites cited and used in the international literature (Hortsch et al., 2023).

Medical students' preferences for microscopic anatomy labs, whether in a distance learning or face-to-face setting, have been a subject of interest, particularly in the context of the COVID-19 pandemic. Studies have explored students' perceptions and attitudes toward online versus traditional teaching methods in anatomy education. For instance, a study by Sarkar et al. (2022) found that more than 90% of students preferred traditional anatomy teaching over online methods, indicating a strong preference for face-to-face interactions in the context of anatomy education. This preference for conventional teaching methods aligns with the sentiment that certain aspects of anatomy education, such as practical lab sessions, are best delivered in a face-to-face setting.

For instance, Gellisch et al. (2022) conducted a randomized experimental field study where medical students attended either regular face-to-face classes for microscopic anatomy or the same practical course online using the Zoom videoconferencing platform. This study provides insights into how students perceive and engage with online versus traditional face-to-face microscopic anatomy classes.

On the other hand, research by Totlis et al. (2021) aimed to determine the impact of the COVID-19 outbreak on anatomy teaching and compared traditional anatomy teaching with remote modalities, highlighting the shift towards online educational methods during the pandemic. This study sheds light on the challenges and adaptations in anatomy education brought about by the pandemic, emphasizing the need to explore alternative teaching approaches to ensure continuity in education. Zarcone & Saverino (2021) detailed experiences during the COVID-19 pandemic, where online platforms like Microsoft Teams and 3D anatomical modeling programs were used for teaching microscopic anatomy. This shift towards online platforms underscores the adaptability of medical education in response to challenging circumstances.

Furthermore, the study by Vinson (2019) emphasized the importance of the anatomy lab experience as a form of professional socialization, where students learn practical skills and interact with peers in a simu-

lated clinical setting. This highlights the unique role of hands-on learning in anatomy education and suggests that face-to-face interactions in the lab setting may offer valuable learning experiences that are challenging to replicate in online environments.

In a study by (Ortadeveci et al., 2022), it was noted that while theoretical aspects of anatomy could be presented remotely, face-to-face teaching was deemed essential for the practical components of anatomy education. This finding underscores the irreplaceable value of hands-on experience in microscopic anatomy labs, where students engage directly with anatomical specimens. Additionally, Cuschieri & Narnaware (2022) emphasized the importance of practical sessions in aiding medical students' understanding of basic sciences like anatomy and retaining knowledge effectively. Practical sessions reinforce theoretical knowledge and enhance students' comprehension of complex anatomical structures.

Overall, the literature suggests that while online platforms offer flexibility and adaptability, there is a strong preference among medical students for face-to-face teaching in microscopic anatomy labs. The hands-on nature of anatomy education, the value of practical experience, and the unique learning environment provided by traditional lab settings contribute to students' inclination towards face-to-face teaching for microscopic anatomy. Balancing the benefits of online and traditional teaching methods is essential to cater to diverse learning preferences and ensure a comprehensive educational experience for medical students.

In conclusion, while there is a growing trend toward incorporating online and remote teaching methods in anatomy education, especially in response to the challenges posed by the COVID-19 pandemic, the preference for face-to-face teaching in microscopic anatomy labs remains strong among medical students. Students value the hands-on nature of anatomical dissection and the interactive learning experiences offered in traditional lab settings. This highlights the importance of balancing technological advancements with preserving practical, experiential learning in microscopic anatomy education.

LIMITATIONS OF THE STUDY

The limited number of students who participated in the study, belonging to only a one-course master's program, represents a limitation of the research, even though this degree program has fewer students enrolled. Further analysis is needed to explain the differences in the usefulness and effectiveness of the two types of

experiences in teaching microanatomy laboratories in a multicenter national study.

AUTHOR CONTRIBUTIONS

Conceptualization, R.M., F.G., B.C.; methodology, F.G, B.C., F.P.; software, C.L., M.S.; validation, B.C., D.O.; formal analysis, B.C; D.O.; investigation, R.M., F.G., M.S; resources, F.G., R.M.; data curation, F.P.; writing—original draft preparation, R.M, F.G ; writing, review and editing, R.M, F.G B.C. D.O.; visualization, F.G., supervision, F.G.; project administration, F.G., R.M.; funding acquisition, RM. All authors have read and agreed to the published version of the manuscript.

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INSTITUTIONAL REVIEW BOARD STATEMENT

Ethical review and approval were waived for this study due to its observance of the Italian University System's evaluation regulations administered by the National Agency for the Evaluation of the University System and Research (<https://www.anvur.it/>, accessed on 03 June 2024) and due to the observance of Sapienza University rules for anonymous students' satisfaction evaluation and Teaching Quality Assessment Questionnaire.

INFORMED CONSENT STATEMENT

Informed consent was obtained from all subjects involved in the study.

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APPENDIX

SECTION A. The virtual microscopy lab.

Questions	1=strongly disagree	2=disagree	3=Neither agree nor disagree	4=agree	5 = strongly agree
A1 How much did you enjoy the virtual microscopy lab experience?					
A2 How helpful was the virtual microscopy lab experience in understanding microscopic anatomy?					
A3 How engaging was the virtual microscopy lab experience?					
A4 To what extent did the virtual microscopy lab experience meet your learning needs?					
A5 How likely will you recommend the virtual microscopy lab experience to other students?					
A6 How comfortable were you with the technology used in the virtual microscopy lab experience?					
A7 How clear were the instructions provided for the virtual microscopy lab experience?					
A8 How sharp were the digital images for the virtual microscopy lab experience?					
A9 How satisfied were you with the virtual microscopy lab experience overall?					

SECTION B. The in-person microscopy lab.

Questions	1=strongly disagree	2=disagree	3=Neither agree nor disagree	4=agree	5 = strongly agree
B1 How much did you enjoy the in-presence microscopy lab experience?					
B2 How helpful was the in-presence microscopy lab experience in understanding microscopic anatomy?					
B3 How engaging was the in-person microscopy lab experience?					
B4 To what extent did the in-presence microscopy lab experience meet your learning needs?					
B5 How likely will you recommend the in-presence microscopy lab experience to other students?					
B6 How comfortable were you with the technology during your in-presence microscopy lab experience?					
B7 How clear were the instructions provided for the in-presence microscopy lab experience?					
B8 How sharp were the images seen with the microscope for the in-presence microscopy lab experience?					
B9 How satisfied were you with the in-presence microscopy lab experience overall?					

SECTION C. in-person vs. remote microscopy

Questions	Preferences
C1 Which experience did you prefer overall?	The virtual microscopy lab experience The in-person lab experience I had no preference.
C2 What did you enjoy about the in-person lab experience? (You may select more than one option)	Having first-hand experience with the light microscope Having been able to see slides in person Having the opportunity to work in groups with other students Having a more interactive experience Other (specify): _____
C3 What did you not enjoy about the in-person lab experience? (You may select more than one option)	The need to be physically in the lab Difficulty using the light microscope or handling glass slides Less flexibility in terms of schedule Other (specify): _____
C4 What did you enjoy about the virtual microscopy lab experience? (You may select more than one option)	The ability to access the lab experience remotely The ability to zoom in and out on images The ability to review the lab experience at your own pace Other (specify): _____
C5 What did you not enjoy about the virtual microscopy lab experience? (You may select more than one option)	Difficulty in using the technology Less interactivity with other students or the instructor Limited ability to ask questions in real-time Other (specify): _____
C6 Which laboratory experience was most helpful in understanding microscopic anatomy?	The in-person laboratory experience The virtual microscopy lab experience. Both experiences were equally helpful. Neither experience was advantageous.
C7 Do you think the in-person laboratory experience provided different educational content than the regular course lecture on microscopic anatomy?	No, it covered the same content as the course lecture. Yes, it covered some additional or more detailed content than the course lecture. Yes, it covered some of the same content as the course lecture, but in a different way or with a distinct emphasis.
C8 Do you think the virtual microscopy lab experience provided teaching content different from the regular course lecture on microscopic anatomy?	No, it covered the same content as the course lecture. Yes, it covered some additional or more detailed content than the course lecture. Yes, it covered some of the same content as the course lecture, but in a different way or with a different emphasis.
C9 Which laboratory experience provided different educational content than the usual lecture on microscopic anatomy?	The in-person laboratory experience. The virtual microscopy laboratory experience. Both experiences provided different educational content. Neither experience provided different educational content.



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Representing the Body. From variety to the perfection of convention: the anatomical plates of the Leonetto Comparini Anatomy Museum, University of Siena

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Abstract. The history of Medicine has been passed down to us through the texts of Anatomy without images from the most ancient periods. Only in the 15th century was Mondino’s work enriched with drawings that went on to explain the dissection methods that the great Bolognese anatomist had included in his book published in 1316. But it was in the 16th century that anatomical drawings assumed extraordinary importance when Andrea Vesalio recognized their extraordinary function in helping to understand the texts and make them accessible to an ever-wider audience interested in the study of Anatomy. The authors, in tracing the highest examples of the history of anatomical iconography for educational use, present the case of the collection of about 600 anatomical plates preserved in the Leonetto Comparini Anatomy Museum of the University of Siena: tables that were made specifically for educational use and that have been regularly used for the teaching of Anatomy throughout the 20th century.

Keywords: anatomical tables, teaching of Anatomy, innovative approach; medical education.

ANATOMY: A VISUAL SCIENCE

The study of anatomy requires the use of visual aids, whether it be a dissected body, a preparation, a model, or a table (1). Images remain at the heart of the anatomy teaching method even today, and the learning of anat-

omy, an objective science, cannot do without the use of “images” (2, 3).

The advice that every teacher gives to students even today in their first lesson is to equip themselves with a good anatomy atlas.

ILLUSTRATORS AND PRINTING TECHNIQUES BEHIND ANATOMICAL PLATES

The need to “see” in order to “learn” has obviously been addressed in different ways in each era. While in the 14th century Mondino de’ Liuzzi (1275-1326) introduced the practice of dissection as a method of investigation and study of the human body, it was in the Renaissance that Andreas Vesalius (1514-1564) introduced a completely innovative method in anatomical teaching methodology and a different way of conceiving anatomical science with his *De humani corporis fabrica libri septem* (4).

The renewed importance of dissection prompted the creation of teaching aids to be used during periods when body dissection was not possible. In particular, anatomical plates, derived from direct observation of the body, were considered more effective than any written text or speech, allowing many people in different places to observe what could only be seen through dissection (5).

Anatomical drawing thus became the most used tool that aided the study and understanding of the human anatomy, which became established in the mid-16th century.

Vesalius’s innovative work, *De humani corporis fabrica* is adorned with the exquisite engravings of the Dutch artist Jan Stephan van Calcar (1499-1546), a Flemish painter trained in Titian’s workshop. These drawings not only exhibit anatomical precision but also stand as masterpieces of art. The human body is depicted in poses reminiscent of classical art, set against beautifully rendered landscapes.

The plates were created using the woodblock printing technique (xylography). The matrix was carved onto a pear wood block. The artist worked on the wooden surface, and then an engraver cut away the areas around the drawing that were meant to remain white, leaving only the image to be printed in relief. The frontispiece and Vesalius’s portrait, which grace the opening pages of *De humani corporis fabrica*, are prime examples of this technique. The frontispiece features the anatomist at the center of the scene, dissecting a female body with his own hands, surrounded by numerous figures of anatomists.

For his revolutionary work, *De Dissectione Partium Corporis Humani Libri Tres*, which features one of the

most elaborate sets of illustrations of the era, Charles Estienne (1504-1564) assembled a team of esteemed illustrators. Among them was Perin del Vaga, a collaborator of Raphael, Rosso Fiorentino, and other masters of the School of Fontainebleau.

Also the famous senese anatomist, Paolo Mascagni (1755-1815), collaborated with highly skilled draftsmen and engravers to produce the exquisite illustrations that adorn his works. Among these artists were Ciro Santi (a Bolognese artist who prepared the copper plates for the illustrations in *Vasorum lymphaticorum historia et ichnographia* (6); Agostino Costa (a Florentine artist who contributed to Mascagni’s works); and Antonio Serantoni (a close collaborator of Mascagni from 1801 to 1815). Serantoni played a pivotal role in creating the illustrations. He prepared the drawings, engraved them on copper plates for printing with etching, and, when necessary, hand-colored them.

The immense work involved in creating these anatomical plates is attested to by the names and signatures placed at the bottom of the plates, within the lower margin of the printed image. These inscriptions are engraved and typically include: the name of the draftsman followed by the term *delineavit* (drew), *delineavit et pinxit* (drew and painted), or in some cases, *delineavit et direxit* (drew and directed); the name of the engraver followed by *sculpsit* (carved) or *incidit* (engraved). In cases where the draftsman and engraver were the same person, the inscription would read *delineavit idemque incidit* (drew and engraved) (7).

These inscriptions serve as a testament to the collaborative nature of anatomical illustration, highlighting the contributions of artists and artisans in bringing scientific knowledge to life through visual imagery.

To produce his plates in a way that would “exhibit the parts of the Human Body by means of new Plates, and present them precisely as they are in nature, preserving the order and respective position of each,” Paolo Mascagni employed a novel technique capable of yielding particularly impressive results: copperplate etching.

In this process, a copper plate was coated with black wax, upon which the image was drawn. Subsequent etching exposed the copper in correspondence with the drawing. Aquafortis, a mixture of nitric acid and water, was poured over the plate to corrode the areas that the etching had stripped of wax. The principle of this technique relies on the protective power of black wax and the corrosive action of a mordant, in this case, nitric acid. Once cleaned, the plate was ready for printing like any other intaglio print. Successive passes on the same plate allowed for further inkings with different colors predominating (7). The use of multiple colors further

enhanced the visual appeal and educational value of the illustrations. It enabled Mascagni to highlight different anatomical features and relationships, making it easier for viewers to understand the complex structures of the human body.

Between the late 18th century and the early 19th century, a new printing process emerged: lithography. This innovative technique utilized a limestone-based stone as the matrix. The artist would draw the image to be printed using greasy ink crayons. The lithographic stone, typically made from limestone, has a remarkable property of retaining a thin film of water on its surface. This water film adheres strongly to the undrawn areas of the stone. When ink is applied to the lithographic stone, it is repelled by the water-covered areas. The greasy ink, however, adheres to the drawn areas, which are free of water. The lithographic process allows for the production of multiple identical prints from the same stone matrix. This reproducibility is a significant advantage of lithography (7).

A FUNDAMENTAL SUPPORT FOR THE TEACHING OF SIENESE ANATOMY

Until few decades ago, the halls of the University of Siena's Institute of Anatomy proudly displayed the magnificent plates of Paolo Mascagni's *Anatomia Universa* (8, 9, 10). Mascagni (11, 12) was born in Siena, had studied at the university and became a young lecturer in anatomy following the death of his teacher, Pietro Tabarrani (1702-1780). *Anatomia Universa* is a life-size atlas that meticulously replicates a dissection, featuring anatomical plates meticulously crafted based on direct observation of the human body. In the preface to this monumental work, Mascagni emphasizes the value of both "verbal descriptions of individual parts" and "using images and representations" in the study of the human body, asserting that "the eyes do not deceive" (8).

Paolo Mascagni's anatomical plates, including those in his *Vasorum Lymphaticorum historia et ichnographia* and *Anatomia Universa*, demonstrate his meticulous attention to detail and leading-edge approach to anatomical illustration. While maintaining a connection to classical iconographic traditions, Mascagni introduced several innovations that reflected a new era in anatomical research and teaching (13, 14).

Mascagni's illustrations are characterized by their clarity and precision. He meticulously depicted anatomical structures with remarkable accuracy, ensuring that students could easily identify and understand the intricate details of the human body. In line with their

didactic purpose, Mascagni's illustrations were free from extraneous elements that might distract from the study of anatomy. He aimed to present the human body as it appeared on the dissection table, allowing students to focus on the essential structures. Mascagni's innovative approach to anatomical illustration marked a significant shift in the way anatomy was taught and understood. His detailed and accurate plates provided students with an unprecedented visual understanding of the human body, revolutionizing anatomical education.

Complementing the collection of antique and precious anatomical plates housed in ornate wood frames and protected under glass, which have been musealized since the late 1990s and can now be viewed in the Natural History Museum of the Siene Academy of Fisiocritici (15), the University of Siena held within its legacy a substantial number of anatomical plates created by lesser-known draftsmen at the explicit request of professors throughout the institution's history. These drawings faithfully reproduce the systems and apparatuses of the human body as they were observed by the technical draftsmen in the Institute of Anatomy, either directly from cadavers or by referencing images from atlases.

These anatomical plates, now replaced in teaching by more modern images, have become part of the heritage of the University of Siena's Anatomical Museum (16, 17, 18). The museum houses a collection of approximately 600 anatomical plates dating from the late 19th century to the 1990s, spanning the period until manual drawing gave way to computer graphics.

This remarkable collection can be divided into two main groups: paper plates, (represent the majority of the collection and showcase the traditional technique of anatomical illustration on paper), and wooden plates (these are distinguished by their unique support material, wood, and provide a glimpse into an earlier era of anatomical illustration).

THE TREASURE TROVE OF ANATOMICAL TABLES

The first group consists of the anatomical tables of the late nineteenth century and are still preserved in their "cassone" (i.e. treasure trove), acquired by the university in 1908. The term "cassone" is a colloquial term for a large chest or trunk, often used to store valuable items (figure 1).

This historical furniture, commissioned *ad hoc*, is made of fir wood, closed by two doors and divided internally in six thematic shelves:

- I: Histology and general physiology;
- II: Embryology;



Figure 1. Furniture specially designed to contain the numerous anatomical tables of the ancient Institute of Normal Human Anatomy of the University of Siena (Museo Anatomico ‘Leonetto Comparini’, Siena).

- III: Digestive system;
- IV: Urogenital apparatus;
- V: Respiratory system;
- VI: Nervous system (19).

The paper tables were used by exposing them in the classroom on a support above the board. If we look at these artifacts we see that they mostly reproduce images of current anatomical atlases. Some have been made in black and white (figure 2) others are in colors (figure 3) often using the watercolor technique.

In any case, we note the artist’s commitment the images a pleasant appearance and to use well-marked strokes in order to make possible remote viewing. In most of these drawings the captions are inserted directly next to the various parts of which the organ is composed (figure 4). Finally, plates are mostly anonymous.

THE ANATOMICAL TABLES OF THE SECOND HALF OF THE TWENTIETH CENTURY

After World War II, anatomy teachers used to prepare specific materials for their lessons, asking technicians to set up the classroom with preparations and anatomical tables depending on the topic they would cover in classrooms.

Many of the anatomical tables used in classrooms were made by the technicians of the Institute itself. Among these deserves to be mentioned Anna Maria D’Errico (20), who began to work in the sixties commissioned by Professor Elio Bagnoli, which was joined by many other teachers such as Sestini, Bertelli, Comparini and Bastianini.

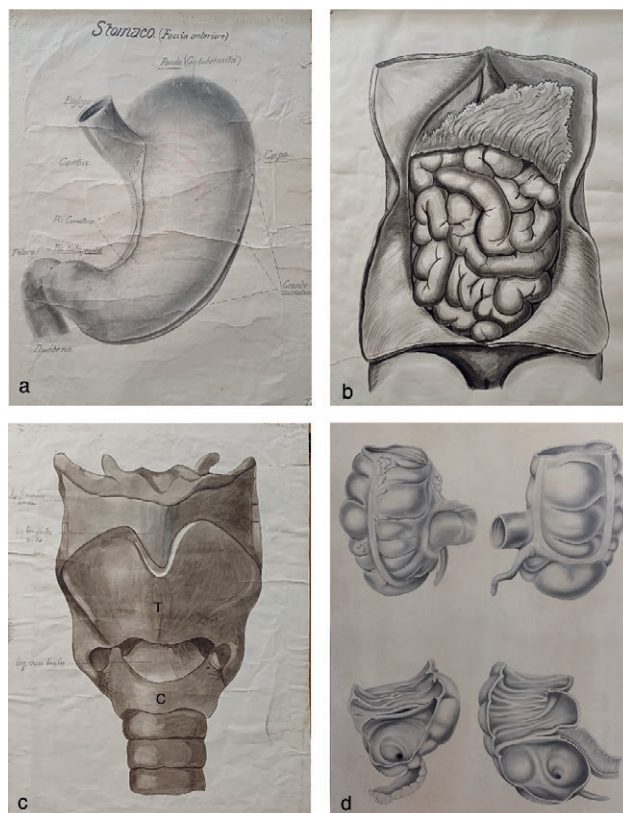


Figure 2. 2a) Stomach in front projection. The various parts that make it up are indicated (bottom and body), the two left and right margins (large and small curvature) and the two orifices, cardias and pylorus that put it in communication with the esophagus and duodenum respectively. 2b) Open abdominal cavity with greater omentum raised, making the mesenterial small intestine visible. 2c) Larynx in front projection. Visible are the thyroid (T) and cricoid (C) cartilages joined by the cricothyroid ligament shown in the table together with the lateral and middle thyroid ligaments connecting the larynx to the hyoid bone. 2d) Terminal part of the ileum that is thrown into the cecum. In the upper left anterior vision, on the right a posterior vision, in both it is possible to observe the humps typical of the large intestine and the ileocecal appendix extending downwards. In the lower part of the table is represented the open cecum, in sagittal section to the left and frontal to the right, where it is possible to observe the ileocecal valve and the opening of the appendix. (Museo Anatomico ‘Leonetto Comparini’, Siena).

In the era before computers, this scientist and artist meticulously has freehand drawing anatomical tables using watercolour, pastel, or tempera techniques. She quickly abandoned ink pens due to the fading of aniline colours over time, especially for exposure to light. As she recalled in a publication on anatomical tables, in her drawings she tried to give a pleasant chromatism and a easily readable illustrations, even from a distance. She performed the captions initially with normographs, later



Figure 3. 3a) Arterial cone of the right ventricle open at the point of origin of the pulmonary trunk with the semilunar valves. It is indicated the left pulmonary artery that originates from the trunk, also the ascending aorta and the superior vena cava are visible. 3b) In high, scheme of the structure of the hepatic lobule with the centrilobular vein blue colored, and the rich system of sinusoids that surround it. Below is a three-dimensional view of the hepatic venous system. 3c) Posterior wall of the thorax. Trachea with bifurcation of the main bronchi are represented. Below a segment of the esophagus. The table shows all the vascular structures surrounding these organs. 3d) Schematization of the course of the optical and acoustic ways with their interrupting nuclei. (Museo Anatomico 'Leonetto Comparini', Siena).

switching on to transferables that gave the work an even more professional look (20).

Her subjects were typically inspired by images from the most important anatomy manuals (Bairati, Pernkopf, Sobotta, Valenti Bertelli) or from teachers' own texts. These drawings were mainly used for classroom teaching but often also for scientific publications. Some of her tables bear her signature, as seen in the black and white illustration of the larynx (figure 5).

Over time, the constant use of the anatomical drawings led to signs of wear and tear. To preserve her work, Anna Maria D'Errico decided to have the drawings lam-

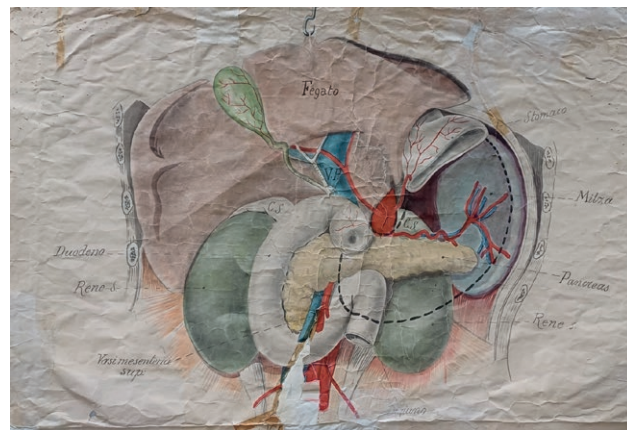


Figure 4. Representation of the retroperitoneal viscera of the upper abdominal cavity: duodenum, pancreas, kidneys with adrenal glands and spleen. (Museo Anatomico 'Leonetto Comparini', Siena).



Figure 5. 5a) Median sagittal sections of the larynx. On the left is represented the upper part of the larynx, in the center the organ in full. On the right are the thyroid cartilages, in front projection, the cricoid and aritenoid cartilages in lateral vision. 5b) On the back of the table is the autograph of the author, Annamaria D'Errico. (Museo Anatomico 'Leonetto Comparini', Siena).

inated and mounted on plywood boards, making them more durable and easier to use in the classroom.

A true professional, D'Errico embraced new technologies as they emerged. She began using a scanner to capture images and then digitally reinterpreted them to meet the specific needs of teachers. However, the arrival of the graphic tablet and Photoshop marked a turning

point for her. As she described, “*it was like going back to drawing with pencil and brush because even in computer graphics, you need to know how to draw, understand perspective, have a sense of colour, and perceive what is most pleasing to the eye and therefore effective for learning*”.

Recent efforts have focused on accurately dating the anatomical tables, identifying missing specimens, and restoring damaged ones.

CONCLUSIONS

For centuries, anatomical tables and drawings have been a cornerstone of anatomy education. This article has explored the collections at the University of Siena, highlighting their enduring value. These meticulous illustrations, crafted by hand or with the aid of evolving technologies, have served as invaluable tools for both students and instructors.

These anatomical tables stand as a testament to the enduring role of visual aids in teaching anatomy. As a descriptive discipline, anatomy heavily relies on illustrations, and these tables have served as invaluable tools for centuries.

The authors, tracing the history of the anatomical didactic tables in use for centuries at the University of Siena, have also sought to highlight the expertise and techniques behind their creation. These tables, as the renowned anatomist Paolo Mascagni recognized, are fundamental instruments for the study of anatomy.

The importance of such a historical heritage also passes through an interpretative reading of the technical and technological evolution. By examining these collections, we gain insights into the history of anatomy and its teaching methods.

The authors emphasize that while the anatomical drawings discussed here may be considered less significant than those of renowned figures like Antonio Scarpa and Paolo Mascagni (also preserved in The Museum of Siena), they nonetheless play a crucial role in anatomy education. Paradoxically, while the importance of dissection was stressed, anatomical teaching has historically achieved its most effective results through the use of visual aids.

Finally, despite the emergence of new technologies in anatomy teaching, the importance of visual aids remains undeniable. These collections offer a unique perspective on the history of the discipline and the artistic expertise required to create effective illustrations.

The story of the collection of the Museum of Siena collections underscores a fundamental truth: even among technologic advances, well-crafted anatomical

tables and drawings continue to be a powerful resource for clear communication and effective learning in the fascinating field of anatomy.

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Accessible anatomy education: the Utibilus Project as a model for inclusive learning

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Abstract. *Background.* Anatomy education, with its dense visual landscapes and intricate terminology, represents a formidable obstacle for all the students but particularly for those with disabilities and specific learning disorders (SLD). Despite legal mandates for equal educational opportunities, the field lacks widespread implementation of effective learning enhancers, jeopardizing inclusivity, and academic success. *Methods.* This study investigated into the pressing need for accessible learning materials in anatomy education. A pilot survey assessed faculty awareness of students with disabilities and SLD within their courses, along with their knowledge and utilization of learning enhancers. To address this gap, the “Utibilus Project” of the University of Pisa developed and implemented a suite of accessible resources, including: 1) Edited PowerPoint presentations with improved layout, enhanced accessibility features, and clear explanations; 2) Implementation of dedicated fonts optimized for readability, reducing visual strain and cognitive load; 3) Comprehensive guidance on accessibility tools like screen readers and mind or conceptual maps, empowering students with diverse learning needs. *Results.* The survey (30.7% response rate) unveiled a concerning lack of faculty awareness regarding the presence and specific needs of students with disabilities and SLD. While most express interest in acquiring further knowledge, their understanding of learning enhancers and their potential to enhance student learning remained limited. The Utibilus Project effectively demonstrated the feasibility and transformative potential of accessible resources. Early data suggested significant improvements in the learning experience for students with diverse needs, particularly in the challenging domain of anatomy education. *Conclusions.* This study underscored the critical and urgent need for accessible learning materials in anatomy education. The Utibilus Project serves as a valuable model, paving the way for a more inclusive and effective learning environment where all students, regardless of individual differences, have equal access to the complex and crucial information within the field. While acknowledging the limitations of the pilot survey, such as its sample size, the findings call for further research to evaluate the long-term impact of these interventions and identify additional strategies to address the specific needs of students with disabilities and SLD in anatomy education. Additionally, exploring the broader benefits of accessible learning materials, such as their potential to improve student engagement and motivation, holds significant promise for enhancing the educational experience for all.

Keywords: accessibility, learning disabilities, specific learning disorders, medical education, anatomy, inclusive teaching, learning enhancers, Utibilus Project.

INTRODUCTION

In Italian universities, participation of students with disabilities, such as low vision, hearing impairment, or deafness, as well as those with specific learning disorders (SLD), is steadily increasing (Istituto Superiore di Sanità, 2021, 2022; ANVUR, 2022). The SLD are classified in the International Classification of Diseases (ICD-11) diagnostic system as a group of neurologically based developmental disorders characterized by significant and persistent difficulties in learning academic skills, including reading, writing, or arithmetic (World Health Organization, 2018). The SLD fall under the broader concept of neurodiversity, which includes various neurological differences such as dyslexia, Attention Deficit Hyperactivity Disorder (ADHD), and autism spectrum disorders (for a review, Clouder et al., 2020). Neurodiversity views these differences as natural variations in human brain function, not as conditions to be treated. Thus, individuals with SLD are seen as neurodivergent, meaning they have different but equally valid cognitive patterns compared to the neurotypical population (for a review, Clouder et al., 2020).

Similarly, over recent years, the percentage of students with SLD enrolled in upper secondary schools has progressively increased (Ministry of Education and Merit, 2020; Ministry of Education and Merit, 2022). Interestingly, the proportion of students with disabilities or SLD is higher in secondary schools compared to universities (ANVUR, 2022; ISTAT, 2024). This discrepancy may be attributed to various barriers that discourage neurodivergent students or with disabilities from pursuing higher education. Factors such as the perception of university studies as excessively challenging, previous negative educational experiences, and a university environment perceived as less inclusive contribute to this issue (Alivernini and Lucidi, 2011; European Agency for Special Needs and Inclusive Education, 2016; Donato et al., 2019).

Furthermore, the transition from high school to university presents a significant change, especially challenging for students with SLD or disabilities (Lithari, 2019; Koutsouris et al., 2021; Parson et al., 2023). These students, accustomed to receiving support from specialized teachers and tutoring programs in their educational backgrounds, may worry about not having access to similar assistance in university. As they move away from a familiar support system, feelings of anxiety and uncertainty may arise, affecting their confidence in achieving success at the university level.

Moreover, some students might opt out of seeking support to avoid potential embarrassment or stigmatization, particularly if they have gone through similar experiences in the past (Pino and Mortari, 2014; Lithari,

2019; Mesa and Hamilton, 2022). This potential scenario could significantly discourage neurodivergent students or with disabilities from enrolling in university courses or even lead them to discontinue their studies if already commenced. Furthermore, if neurodivergent or disabled students do not have, or are not enabled to have, adequate knowledge of the services and support offered by universities in terms of insufficient inclusivity, they may develop a detrimental sense of inadequacy (ANVUR, 2022). Consequently, this situation could dramatically dissuade these students from continuing their university courses or push them to prematurely interrupt their studies if they have already started.

A crucial aspect of the educational process that can profoundly influence students' academic paths is the hidden curriculum. This concept refers to the set of expectations, values, and norms that govern behavior and interaction in universities, implicitly conveyed through the institution's environment and culture, beyond formal lessons (Alsubaie, 2015; Koutsouris et al., 2021). Thus, the hidden curriculum contributes differently from the formal curriculum to the overall development of students, affecting their self-perception and abilities (Alsubaie, 2015; Koutsouris et al., 2021; Hamilton and Petty, 2023). Given its implicit nature, the hidden curriculum can present a significant challenge for students with neurodivergent conditions or disabilities, generating or exacerbating feelings of inadequacy, isolation, and frustration (Sulaimani and Gut-Zippert, 2019; Koutsouris et al., 2021; Hamilton and Petty, 2023).

Therefore, it is essential for educational institutions to recognize the impact of the hidden curriculum on these individuals and take concrete steps to mitigate its potential negative effects.

Personal and family expectations also play a crucial role, as a supportive and understanding family environment significantly influences students' self-esteem and academic success (Syeda and Batool, 2020). Additionally, many students with disabilities or SLD face mental health challenges, such as anxiety and depression, which further complicate their educational path (Ghisi et al., 2016; Chieffo et al., 2023). Overall, students with neurodivergent conditions or disabilities may perceive the university environment unwelcoming due to various factors, feelings, or prejudices. These include a lack of knowledge about available support/services, a stressful transition, academic and logistical challenges, low self-esteem, social or familial pressures, and experiences or fear of discrimination and stigma. Individually or collectively, these factors can lead to a sense of inadequacy, ultimately discouraging these students from embarking on or continuing higher education.

The challenges encountered by students with neurodivergent conditions or disabilities in accessing higher education underscore the significance of fostering an inclusive educational setting, a principle strongly advocated by the United Nations Convention on the Rights of Persons with Disabilities, adopted on December 13, 2006, under resolution 61/106 (United Nations, 2006). This convention was ratified by Italy in 2009, reaffirming the nation's commitment to ensuring equal educational opportunities for all individuals (Italia, 2009). Italian laws No. 104/1992, No. 17/1999, and No. 170/2010 are specifically addressing disabilities and SLD to ensure the right to education, promote equality across all educational institutions, and establish standards for personalized support services, ensuring that all the students receive the necessary assistance to excel academically (Italia, 1992, 1999, 2010). More recently, the protection of the right to education for students with SLD has been reinforced, outlining methodologies for educational support and training for teachers, including those in universities (Ministero dell'Istruzione, 2011). Finally, guidelines to further enhance inclusive practices for students with SLD have been updated by the National University Conference of Delegates to Disability (CNUDD, 2014; available at <http://www.cruil.it/documenti-pubblici.html>).

Challenges faced by students with SLD in the study of human anatomy in Medicine and Surgery programs

Within the context of Medicine and Surgery degree program, students with SLD may encounter significant challenges in studying human anatomy. These challenges are characterized by the need to grasp the knowledge of complex anatomical structures and their three-dimensional interrelationships within the human body. In this regard, students with SLD may struggle with visualizing and mentally manipulating these structures, potentially impacting their comprehensive understanding of morphological and functional anatomical concepts.

Additionally, the need to memorize and accurately utilize the extensive, detailed, and specific range typical of anatomical nomenclature can pose a significant obstacle for students with SLD, especially those who have difficulty understanding spatial and visual information. This latter aspect may stem from the educational materials provided to them, even during frontal lectures.

Furthermore, it is well-known that the practical application of anatomical knowledge, understood as the translation of theoretical knowledge into practical skills in a clinical context, is a cornerstone of competence that a student in the Medicine and Surgery degree program must acquire. SLD students may encounter difficulties

in translating their theoretical knowledge into practical skills, especially if they struggle to integrate information from various sources that may not be fully accessible. This risk becomes particularly realistic if the educational materials provided by professors to students, whether they are individuals with SLD or not, have not been created with criteria aimed at improving their usability. It is evident, therefore, that the teacher plays a crucial role in engaging students in an inclusive educational journey that involves removing obstacles hindering learning to ensure all students have access to and full mastery of the educational material.

In light of these considerations, our group has developed the Utibilus Project, a collection of tools aimed at disseminating effective methodologies (best practices) to enhance the learning process for all students, particularly those with neurodivergent conditions or disabilities. As part of the project, a survey has been conducted as a pilot analysis to assess the faculty of the School of Medicine at the University of Pisa regarding (1) their level of awareness of the presence of individuals with neurodivergent conditions or disabilities in their teaching courses, and (2) their level of knowledge about tools, methodologies, and strategies suitable for creating educational materials of excellent usability, and the potential these may express, if correctly utilized, as integral components of educational tools to enhance the learning process for all students, particularly those with neurodivergent conditions or disabilities.

METHODS

The Utibilus Project (from Latin: *utibilus*, meaning "more useful and advantageous" as superlative of *utibilis*), was conceived within the School of Medicine with the aim of providing methodologies and tools to enhance the accessibility and effectiveness of educational materials offered in the medical degree program. Improving the accessibility and effectiveness of educational materials is crucial for ensuring that all students have equal opportunities to learn and succeed. This goal is particularly significant in teaching disciplines that are highly complex and challenging, such as human anatomy, which poses difficulties for many students. Therefore, enhancing the accessibility and effectiveness of educational materials can significantly alleviate these challenges, which may sometimes impede the learning process. Indeed, by improving the accessibility of materials -such as providing visual teaching tools, or material edited in a more user-friendly manner- lectures can assist all students, regardless of learning disabili-

ties, in better understanding complex concepts, leading to positive outcomes in terms of knowledge quality and, consequently, medical practice. Therefore, investing in improving the accessibility and effectiveness of educational materials, especially in disciplines like human anatomy, is crucial for promoting inclusive learning environments and fostering the success of all students in their academic and professional endeavors.

Within the scope of the Utibilus Project, a range of tools has been developed, such as PowerPoint presentations, materials in PDF format, and video clips, to disseminate effective methodologies and procedures -i.e. best practices- aimed at enhancing the learning experience for all students, specifically those neurodivergent conditions or disabilities. In particular, the project has identified five key areas of development:

1. Promoting the use of inclusive fonts to enhance the readability of educational materials (Schneps et al., 2013; Rello and Baeza-Yates, 2016; Bachmann and Mengheri, 2018)
2. Encouraging the adoption of proper formatting techniques to improve the readability of educational materials (Martelli et al., 2009; British Dyslexia Association, 2023)
3. Implementing the integration of the accessibility checker available in Microsoft 365 Office to ensure that educational materials are accessible to all students, including those with disabilities or SLD (Microsoft, 2024)
4. Advocating for the use of mind maps and concept maps as suitable instructional tools to promote deeper conceptual understanding (Johnston, 2019)
5. Introducing assistive technologies, such as screen readers, to ensure equal learning opportunities for all students (Dawson et al., 2018)

As an additional objective of the Utibilus Project, a pilot survey was conducted to evaluate (1) the level of awareness among the faculty of the School of Medicine regarding the potential presence of individuals with neurodivergent conditions or disabilities who actively attend their courses, and (2) the level of knowledge and potential utilization of methodologies, procedures, or technological tools aimed at enhancing the accessibility and usability of educational materials commonly available to students in the university academic setting. For this purpose, a questionnaire was prepared using Google Form, consisting of 25 questions (see Table 1). All faculty of the School of Medicine was invited via email (with 2 invitations sent one week apart) to participate voluntarily and completely anonymously.

RESULTS

The findings from the questionnaire distributed among the 270 faculty members of the School of Medicine, with 83 responses collected (30.7%), offer valuable insights into the knowledge and utilization of tools aimed at improving the accessibility of educational materials, particularly for students with neurodivergent conditions or disabilities.

Understanding of accessibility tools and methods

Upon analyzing responses, a diverse picture emerges. Only a negligible 2% of faculty members regard themselves as “highly” proficient, while a significant 48% claim to possess “moderate” knowledge. Nonetheless, concerning is the fact that 33% perceive their knowledge as limited, with an additional 7% admitting to a complete lack of understanding.

Awareness of students with SLD or disabilities

When examining the involvement of students with SLD in educational activities, 39% of faculty members acknowledge being aware of their presence in their courses. However, a significant gap in awareness exists: 44% of faculty members are unaware of the presence of students with SLD in their classes, and only 17% report negatively. A similar pattern emerges for students with disabilities. About 32% of faculty members recognize their presence, while 47% are uncertain, and 21% report negatively.

Evaluation of educational material adequacy

An intriguing observation arises concerning the perception of the adequacy of educational material for students with SLD or disabilities: 42% of faculty members believe their material to be adequately accessible, while 45% express uncertainty regarding its accessibility. Surprisingly, only 13% consider the material to be insufficiently accessible.

Accessibility checks

Remarkably, the majority of faculty members, constituting 74%, have never conducted accessibility checks on their educational material, with only 26% having done so.

Familiarity with Microsoft Office accessibility tools and inclusive fonts

It is surprising to note that a substantial majority of faculty members, accounting for 83%, are unaware of Microsoft Office’s capability to conduct accessibility checks on created documents. Similarly, awareness of fonts that can enhance text readability is limited, with only 30% of faculty members familiar with such fonts and a mere 22% incorporating them into their documents.

Understanding of guidelines or best practices

A concerning revelation surfaces concerning awareness of guidelines or best practices for creating accessible educational material, with a notable 80% of faculty members lacking awareness. In contrast, only 20% are informed about these practices, revealing a clear knowledge gap necessitating targeted training interventions.

Understanding and use of conceptual and mind maps

A significant deficit is observed in the understanding and utilization of conceptual and mind maps among faculty members. 65% are unaware of the distinction between a conceptual map and a mind map. Additionally, only a mere 17% have ever created or used such maps in their professional activities. Moreover, the use of dedicated software for their creation is exceedingly limited, with only 2% of faculty members utilizing it.

Understanding and use of voice synthesis tools

A notable deficit emerges in the understanding and use of voice synthesis tools among faculty members. A significant 87% are unaware of programs enabling text identification and interpretation through voice synthesis. Moreover, only a modest 25% are aware of the Text-To-Speech functionalities integrated into the Microsoft Office programs currently in use.

Interest in further information

It is encouraging to note that 96% (n=80) of faculty members have expressed a strong interest in receiving additional guidance on how to make their educational materials more accessible. When asked to indicate by which method they prefer to be informed, Powerpoint presentations and video tutorials received the most preferences (see Figure 1).

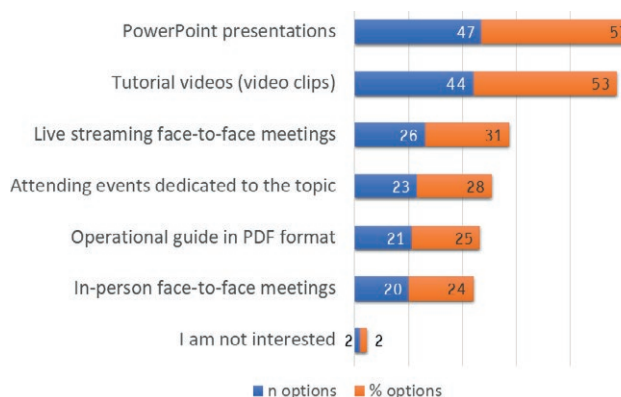


Figure 1. How survey participants prefer to receive information (graph from PowerPoint)

DISCUSSION AND CONCLUSIONS

The growth of students with disabilities and SLD in Italian universities

In the academic year 2019/2020, students with disabilities or SLD constituted 2.13% of the total student population in Italian universities, including both public and private institutions (ANVUR, 2022). Notably, within public universities, the enrollment of students with disabilities experienced a substantial increase, quintupling from approximately 4,400 in the academic year 1999/2000 to around 20,000 (19,875) in 2020/2021 (ANVUR, 2022). However, over the past nine years, there has been a more pronounced increase in the enrollment of students with SLD, rising from around 1,000 (ANVUR, 2022) in the academic year 2011/2012 to approximately 20,000 (19,616) in 2020/2021 (ANVUR, 2022). Given these statistics and the current trends, the number of university students with SLD is expected to surpass those with other disabilities in the coming years (ANVUR, 2022). It is interesting to note that in the Italian educational landscape, the percentage of individuals with disabilities or SLD enrolled in universities is lower than that of those enrolled in secondary schools.

Trends in enrollment of students with disabilities and SLD in Italian upper secondary schools

Data from the Italian National Institute of Statistics (ISTAT) indicates that in Italian upper secondary schools, the percentage of students with disabilities has steadily increased over the last ten years, rising from 2.3% in 2015/2016 to 2.9% in 2019/2020, to 3.0% in the following year (ISTAT, 2021), and finally to 4.1% in 2022/2023 (ISTAT, 2024). Similarly, the percentage of

students with SLD enrolled in upper secondary schools has also progressively increased over recent years. It rose from 4.7% in the 2017/2018 school year (Ministero dell'Istruzione, 2019) to 5.3% in 2018/2019 (Ministero dell'Istruzione, 2020), to 5.9% in 2019/2020, and to 6.3% in 2020/2021 (Ministero dell'Istruzione, 2022).

Barriers to higher education for students with disabilities and SLD

The lower percentage of individuals with disabilities or SLD in university courses compared to upper secondary schools may stem from various factors influencing the decision not to pursue higher education (Dumitru, 2023). These factors could include prejudicial considerations -university studies considered too difficult and concern of failure-, past negative experiences, or perceptions of the university environment as less inclusive and motivating (Alivernini and Lucidi, 2011; European Agency for Special Needs and Inclusive Education, 2016; Donato et al., 2019).

Firstly, it can be argued that the higher prevalence and percentage of individuals with disabilities or SLD in high schools compared to universities may result, at least in part, from increased awareness and advancements in the diagnosis of these conditions in recent years. Diagnoses often occur during school age, leading to higher identification rates in secondary education. In other words, the current differences might be rooted in the fact that students in primary and secondary schools are now more likely to be diagnosed with disabilities or SLD than those who attended these schools in the past and are now at university.

Secondly, it is crucial to recognize that the transition from high school to university represents a significant period of change, particularly daunting for students with disabilities or SLD. Students who have received support from specialized teachers, tutoring programs, and curriculum adjustments in high school could fear the lack of similar assistance at the university level. Moreover, it is important to consider that many students may prefer to give up the opportunity to receive support to avoid embarrassment or stigmatization, especially when they have suffered these effects in previous school experiences (Pino and Mortari, 2014; Lithari, 2019; Mesa and Hamilton, 2022). Additionally, limited access to information on available services and supports for students with disabilities or SLD in universities could leave these students unprepared to confidently face the increased autonomy, time management, and academic workload required by university studies (ANVUR, 2022). This could lead to deleterious effects, such as students with disabilities

or SLD choosing not to enroll in university courses or interrupting their studies if they have already begun.

Thirdly, personal and family expectations could significantly influence the decisions of students with disabilities or SLD regarding university studies. A positive, supportive, and compassionate parenting style has a significant impact on the self-esteem of university students, and self-esteem significantly mediates between positive parenting, academic procrastination, and academic achievement (Syeda and Batool, 2020).

Finally, it is crucial to acknowledge that adolescents with disabilities or SLD often grapple with health issues such as anxiety and depression (Nelson and Gregg, 2012; Nelson and Liebel, 2018; Chieffo et al., 2023). Notably, a gender-based effect was observed, with females with dyslexia reporting a higher incidence of depression and anxiety symptoms compared to their male counterparts (Nelson and Gregg, 2012). A comparable scenario has been noted in the university environment, where students with dyslexia tend to report a greater number of psychological issues, such as low self-esteem, poor resilience, and symptoms of depression and anxiety, compared to students without dyslexia (Ghisi et al., 2016).

In summary, it can be argued that individuals with a disability or SLD may perceive the university environment as unwelcoming due to a combination of factors, including lack of support, a stressful transition, academic and logistical barriers, low self-esteem, social and familial pressures, inadequate information and awareness, and experiences of discrimination and stigma. These factors could contribute to a sense of inadequacy that discourages students with disabilities or SLD from pursuing higher education.

The legislation promoting inclusive education

On December 13, 2006, the United Nations General Assembly formally adopted the Convention on the Rights of Persons with Disabilities (CRPD) under resolution 61/106 (United Nations, 2006). This treaty underscores the importance of acknowledging the right to education for individuals with disabilities and advancing an inclusive educational system (Article 24.1). Additionally, it calls upon Member States to enact measures that promote the use of alternative communication methods, educational techniques, and materials to support persons with disabilities (Article 24.4). Italy ratified the Convention through Law No. 18/2009 (Italia, 2009).

Italian legislation on disabilities, including SLD, is primarily governed by Laws No. 104/1992, No. 17/1999, and No. 170/2010 (Italy, 1992, 1999, 2010). These laws protect the right to education for individuals with disa-

bilities and promote equality across all educational institutions, including universities. They also establish standards for personalized support services, ensuring that students with disabilities receive the assistance they need to succeed academically. Law No. 170/2010 focuses on SLD and enhances the educational rights of affected individuals by providing tailored support, including dispensatory tools and/or compensatory measures, to address academic challenges and promote success.

Subsequently, Ministerial Decree no. 5669/2011 further safeguards the right to education for students with SLD, outlining educational and didactic support methodologies, along with training procedures for teachers, including those operating within university settings.

More recently, the CNUDD updated its guidelines (<https://www.crui.it/documenti-pubblici.html>) adding a section dedicated to SLD students in which the general references for inclusive practices are redefined (CNUDD, 2014).

The analysis of survey responses highlights the need for improvement initiatives to promote a more inclusive and accessible educational environment within the School of Medicine. Specifically, four key areas emerge as interconnected and fundamental to achieving this goal.

Firstly, promoting targeted training programs is crucial to encourage the adoption and use of methodologies, procedures, and tools capable of creating more accessible and usable educational materials for the entire student community. This is particularly critical for students who struggle with poorly formatted or inadequately edited educational content. Such initiatives would ensure that the educational needs of neurodivergent students or those with disabilities are properly addressed.

Additionally, faculty members, especially those teaching challenging subjects such as human anatomy, should receive training to accommodate diverse learning needs. This would enable them to implement and promote the use of appropriately formatted materials, visual aids, mind maps, or alternative assessment methods in their teaching, thereby enhancing inclusivity and accessibility in the learning process.

Simultaneously, introducing initiatives that provide opportunities for assessing and evaluating the adequacy of educational materials and teaching practices, including incorporating student feedback, would make educational materials more inclusive and accessible for all students, especially those with visual impairments or dyslexia.

Lastly, the lack of accessibility checks for materials produced (e.g., slides or .doc documents) by the vast majority of faculty members underscores the need to

improve familiarity with Microsoft Office accessibility tools (Microsoft, 2024). Organizing workshops and informative sessions focused on understanding and appropriately using these tools and procedures could significantly enhance faculty awareness of document and presentation accessibility.

Thus, developing and disseminating guidelines or best practices for creating accessible educational materials is an important objective that requires attention to promote a more inclusive and accessible educational environment within the School of Medicine. Addressing these four interconnected key areas represents a crucial step in this direction.

The Utibilus Project

The project has aimed to develop a repertoire of tools, including presentation software, PDF documents, and video clips, to create opportunities for access to best practices and guidelines to facilitate the production of materials that ensure equal access to educational resources for all students (British Dyslexia Association, 2023). Within the project, we highlighted best practices in correct editing and formatting for dyslexia-friendly features. This includes proper line spacing, inter-letter spacing, inter-word spacing, optimal line length, maximum number of lines, and maximum number of words per line on a single slide (Martelli et al., 2009; Zorzi et al., 2012; Gori and Facoetti, 2015; Damiano et al., 2019; Galliussi et al., 2020; British Dyslexia Association, 2023). Attention was also given to text justification, appropriate font sizes, and the selection of inclusive fonts (Schneps et al., 2013; Rello and Baeza-Yates, 2016; Hakvoort et al., 2017; Bachmann and Mengheri, 2018; Damiano et al., 2019). All these strategies allow to enhance readability and reduce visual stress for students with dyslexia or other reading difficulties. With the Utibilus Project we aimed to contribute to the creation of a more inclusive and accessible learning environment for all students, regardless of their individual learning needs or abilities. To achieve this goal, and considered the preferences expressed by the faculty on the methods that they would have preferred to be informed by, we have developed PowerPoint presentations and short video tutorials that comprehensively outline the steps for installing inclusive fonts, properly editing and formatting slides and textual documents, creating mind maps and concept maps, and conducting accessibility checks for educational materials.

The analysis of responses to the open-ended question regarding the measures taken by faculty to enhance the accessibility of educational materials has uncovered a broad spectrum of strategies employed, some of which

prove suitable for the purpose, while others are wholly or partially inadequate. Moreover, there is considerable variability in individuals' awareness of the importance of accessibility.

Many professors reported providing educational materials to their students in various formats, such as video recordings and PDF slides, yet they failed to provide details on the editing and formatting criteria applied for their creation. Some professors mentioned using fonts and colors that, in their view, enhance readability. Many indicated their aim to simplify content using "clear and concise" language, avoiding "complex terms," and incorporating visual aids like images and diagrams. However, some instructors admitted to not employing specific strategies to improve accessibility, citing a lack of knowledge about the types of disabilities among their students. Others, finally, reported not having specific strategies in place but being open and willing to learn more about accessibility.

Overall, therefore, there is a widespread willingness on the part of professors to implement strategies to improve accessibility, although the need for greater awareness and training on this topic to effectively meet the diverse needs of our students remains marked, thus ensuring equal opportunities for success across the board.

Therefore, the analysis of the questionnaire responses highlights several critical areas that need addressing to improve and ensure a more inclusive and accessible educational environment within academia. These gaps can be addressed through the dissemination and implementation of appropriate tools to enhance the accessibility and usability of educational materials. Achieving this goal is pivotal in academic education to ensure equal learning opportunities for all students, particularly those who are neurodivergent or have disabilities.

Promoting inclusivity through a shift in perspective

The responses provided by the faculty of the Medical School to the questionnaire highlight a lack of awareness regarding the tools, methodologies, and procedures necessary to improve the accessibility of educational materials for all students, whether they are neurotypical, neurodivergent, or have disabilities. This gap could only be bridged through the implementation of specific and effective support and training initiatives, enabling faculty members to create more inclusive and accessible educational materials, thereby enhancing the learning process.

In this context, it is crucial to emphasize that at present, the professors lack the ability to determine if there are neurodivergent students or those with disabilities in their classrooms. The existing legislation does

not mandate the disclosure of such information, which serves to protect privacy rights and mitigate the risk of stigma. Nonetheless, this circumstance may result in the presentation of educational materials that are potentially inaccessible.

Therefore, it would be advisable to consider the opportunity to completely overturn the approach followed up to now. It would be significantly more beneficial, not just for neurodivergent or disabled students but for the entire student community, if faculty were willing to see their classrooms as potentially including students with diverse needs, without needing direct confirmation of this. As widely recognized, paying careful attention during the editing and formatting of educational materials can greatly improve usability and accessibility for all users, including those who are neurodivergent or disabled (Schneps et al., 2013; Rello and Baeza-Yates, 2016; Hakvoort et al., 2017; Bachmann and Mengheri, 2018; Damiano et al., 2019; Galliussi et al., 2020). If we adopted this perspective, we would feel ethically obligated to implement procedures to improve the accessibility and usability of educational materials for all students. This approach would not only be desirable but indeed necessary, as qualitative improvements in the material would benefit all students, whether they are neurodivergent, disabled, or not.

Interestingly, to enhance inclusivity in universities and bridge the gap between students with and without dyslexia, a recent machine learning model has been developed to estimate the most suitable support methods for dyslexic students (Zingoni et al., 2024). This approach facilitates the customization of educational activities to meet each student's specific needs, offering tools and strategies tailored to the challenges encountered throughout their university journey.

Breaking down barriers to empathy and inclusivity in human anatomy

Viewing classrooms as potentially accommodating students with diverse needs, including those who may be neurodivergent or have disabilities, would not only be desirable but also essential, as qualitative improvements in materials would benefit all students, regardless of their neurodiversity or disability status. The adoption and application of this paradigm appears particularly desirable, especially for the teaching of those disciplines that are considered particularly challenging, such as human anatomy traditionally is within the context of the medical degree course.

In conclusion, within the context of the Medicine and Surgery degree program, teaching human anatomy

necessitates every effort to ensure maximum accessibility and inclusivity of educational materials. This entails adopting pedagogical approaches that consider the diverse learning needs of students and ensuring that the educational content is accessible to everyone, regardless of any disabilities or language barriers. This fosters the creation of an inclusive learning environment where every student feels respected and supported in their academic path (Fitzpatrick and Barrett, 2023). Such an approach not only enhances students' educational experience but also helps to cultivate more empathetic and aware healthcare professionals who understand the challenges associated with accessibility in the healthcare setting.

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Table 1. Survey on School of Medicine Faculty awareness and use of educational material accessibility enhancement tools.

-
1. How much do you consider yourself knowledgeable about methods and tools aimed at improving the accessibility of educational materials? (*)
 2. Do students with SLD participate to the lessons of your teaching course? (**)
 3. Do students with some form of disability participate to your course lessons? (**)
 4. If you answered affirmatively, do you know what disabilities they have (e.g., auditory, motor, visual)? (‡)
 5. Do you think your educational material is adequately accessible to students with SLD or disabilities? (**)
 6. Have you ever conducted an accessibility check on your educational material? (**)
 7. Do you know that Microsoft Office you currently use (Word, PowerPoint, Excel) allows you to check whether the document created has accessibility problems? (\$)
 8. What measures do you take in preparing lessons for your teaching course to improve the accessibility of educational material? (‡)
 9. Do you know if there are fonts that can improve text readability for individuals with dyslexia? (\$)
 10. If you answered affirmatively, can you indicate which ones you are aware of? (‡)
 11. Do you use fonts in your Word, PowerPoint, or Excel documents that can improve text readability for individuals with dyslexia? (\$)
 12. If you answered yes, can you indicate which one you use? (‡)
 13. Are you aware of any guidelines or best practices for creating educational material (e.g., slides) that make text reading easier? (\$)
 14. If you answered affirmatively, can you indicate which ones you use most frequently for preparing your educational material? (‡)
 15. Do you know the difference between a concept map and a mind map? (\$)
 16. Have you ever created and/or used mind maps or concept maps in your professional activity? (\$)
 17. Do you use software programs and/or websites for creating concept maps? (\$)
 18. Do you use software programs and/or websites for creating mind maps? (\$)
 19. If you answered affirmatively, can you indicate which ones? (‡)
 20. Are you familiar with programs that allow for the identification and interpretation of text displayed on a computer monitor and present it via speech synthesis? (\$)
 21. If you answered yes, can you indicate which one you know? (‡)
 22. Do you know if the Microsoft Office programs you currently use (e.g., Word, PowerPoint, Excel) include default Text-To-Speech functionality tools to reproduce written text as spoken words? (\$)
 23. Would you like to receive more guidance on methodologies to improve accessibility to your educational material? (\$)
 24. Indicate through which method(s) you would prefer to be informed
 - a. PowerPoint presentations
 - b. Operational guide in PDF format
 - c. Tutorial videos (video clips)
 - d. Live streaming face-to-face meetings
 - e. In-person face-to-face meetings
 - f. Attending events dedicated to the topic
 - g. I am not interested
 25. Indicate any other preferred methods (‡)
-

Note:

(*) answer using a 5-point Likert scale, where 1 represents “Not at all” and 5 represents “Very Much”

(**) Answer using “Yes,” “No,” or “Don’t know”

(\$) Answer using “Yes,” or “No”

(‡) Open-ended response

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