CardioGenesis4D: Interactive Morphological Transitions of Embryonic Heart Development in a Virtual Learning Environment

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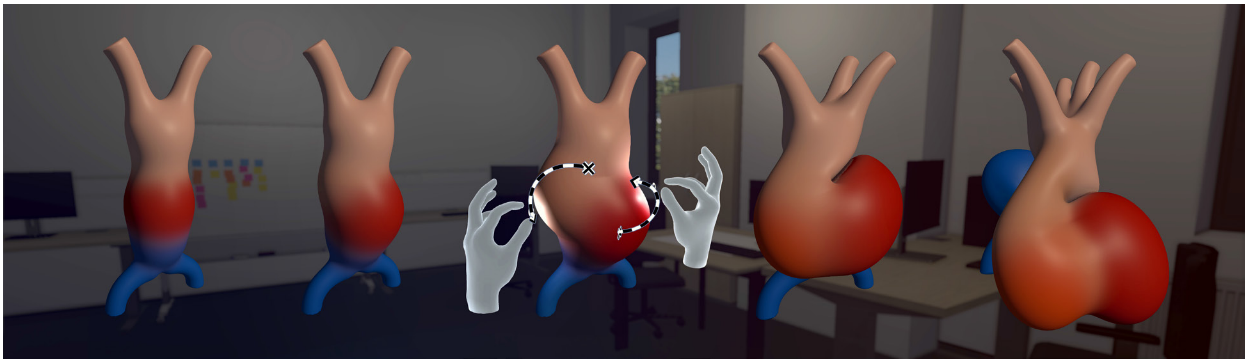

Fig. 1: A collage of multiple stages of the transformation of the heart tube during embryological cardiogenesis as seen in the VRLE. The center heart shows the transformation in progress: the tracked hands of the user follow the arrows indicating growth directions.

Abstract—In the embryonic human heart, complex dynamic shape changes take place in a short period of time on a microscopic scale, making this development difficult to visualize. However, spatial understanding of these processes is essential for students and future cardiologists to properly diagnose and treat congenital heart defects. Following a user centered approach, the most crucial embryological stages were identified and translated into a virtual reality learning environment (VRLE) to enable the understanding of the morphological transitions of these stages through advanced interactions. To address individual learning types, we implemented different features and evaluated the application regarding usability, perceived task load, and sense of presence in a user study. We also assessed spatial awareness and knowledge gain, and finally obtained feedback from domain experts. Overall, students and professionals rated the application positively. To minimize distraction from interactive learning content, such VRLEs should consider features for different learning types, allow for gradual habituation, and at the same time provide enough playful stimuli. Our work previews how VR can be integrated into a cardiac embryology education curriculum.

Index Terms—Virtual Reality, Immersive Learning Environment, Embryonic Heart Development, Anatomy Education

1 Introduction

Embryology is the branch of anatomy that deals with human development in the womb. It allows us, through the study of the developing embryo, to understand both the form and function of the anatomical structures. Furthermore, it is crucial for the understanding of congenital diseases. It thus lays the foundation for the anatomical knowledge of medical students. However, understanding embryology in terms of embryonic development (embryogenesis) and, in particular, the formation of organ systems (organogenesis) is difficult due to the lack of three-dimensional (3D) orientation [30]. This is because simultaneous growth processes and rapid 3D change take place within a short period of time [1, 9]. The embryonic heart undergoes complex morphological transitions and changes shape several times within a few days. Understanding these processes is essential for students and later, cardiologists to properly diagnose and treat congenital heart defects. After all, it is in the process of shape change and its weak points where the causes of most pathologies lie. Previous learning tools, such as 2D representations in textbooks, videos or 3D models, are therefore limited, as the dynamic internal and external developments within this process cannot be taken into account.

The use of virtual reality (VR) as a teaching modality can enhance the understanding of complex spatial relationships through improved depth perception, immersion, and sense of presence [31]. The high level of immersion in VR can provide new and intense learning experiences. Interactive 3D visualizations enable learners to develop mental models of complex, anatomical regions [32]. For this reason, the number of VR applications for teaching in medical education has greatly increased [11, 25]. While anatomy is an essential foundation and students find it exciting and practical, embryology does not enjoy great popularity because it is intangible and therefore more difficult to understand. In addition, embryology constitutes only a small part of the curriculum, and the cardiovascular system in particular is not well emphasized.

To engage students in this topic, we have developed a virtual learning environment (VRLE) in the context of embryonic human heart development based on expert interviews and in collaboration with cardiologists. We address individual learning types by implementing different features and gamification elements. By integrating advanced interactions and dynamic visualizations, users have the opportunity to explore four-dimensional (4D) morphological changes through deformable organ models and better understand temporal evolution.

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Within this research project, we first saw the necessity to create a user-friendly basis and only then to investigate actual effects on learning behavior. Therefore, in this initial step, we were first interested in usability and presence aspects of the development of such an application. To this end, our investigation includes experienced and inexperienced users of VR applications. Learning aspects were, consequently, only secondarily considered in a small sample. In this context, this works research question was raised, how suitable forms of representation and interaction of the temporal development of the embryonic heart can be presented.

2 Related Work

This work investigated potentials of employing immersive VR technology in human embryology teaching. The following outlines the state of the art in the general field of immersive learning and details current practices in embryology teaching.

2.1 Immersive Learning

Immersive learning experiences and the use of VRLE in education to increase engagement and retention have been described by De Freitas et al. [13]. In their study, an evaluation methodology is proposed to support the development of learning activities in virtual worlds. The authors decipher that increasing interactivity creates new experiential learning circumstances in virtual and hybrid spaces, develops complex social interactions, and thus promotes learner ownership. Integrating VR into higher education is a challenge that was highlighted by Jin et al. [24] and Ripka et al. [34] because of the need to consider the perspectives and requirements of various stakeholders and the individual conditions involved. Immersive VR environments as educational tools for anatomy learning are gaining popularity as a replacement for the conventional use of cadavers [39] and can improve students' test scores [26]. Augmented reality (AR) systems can be used for a group of learners in a dissection course and has the potential to meaningfully supplement the learning of anatomy [6]. The advantages of combining 3D autostereoscopic visualizations and gesture interaction for anatomy learning spaces, are presented by Zhang et al. [44]. Thus, their multi-user environment can be used to provide students with morphological differences (health and disease) based on interactive adaptation of original medical images. Important developments such as collaborative multi-user VR learning scenarios based on encountering and interacting with original medical data over distances between students and instructors in a single environment are reviewed by Schott et al. [37].

Falah et al. [14] introduced an interactive VR and 3D visualization system which provides self directed learning and assessment of adult human cardiac anatomy using semi-immersive stereoscopic displays and projections. A comparative study between the VR heart anatomy system and traditional medical teaching modalities (physical heart model) showed that VR learning improved student understanding of heart anatomy by offering an enhanced experience [3]. It also demonstrated the usefulness of the system by showing a higher satisfaction rate regarding structure and visualization. Maresky et al. [29] visualized CT and MRI data of normal and near-normal adult hearts in "The Body VR: Anatomy Viewer" in combination with anatomical models in "Sharecare VR" to create a unique cardiac virtual environment. A pilot study with undergraduate medical students for evaluation demonstrated the viability and the effectiveness of VR in teaching cardiac anatomy. Anderson et. al. [4] commented on the excellence of their pedagogical approach but questioned the anatomical correctness of the models used in the study of Maresky et al. showing the high difficulty of creating appropriate material for virtual learning environments that hold up to the high standards of medical science. The creation and rearrangement of cardiovascular structures by learners in a virtual space is beneficial to the spatial understanding of complex anatomy and can be realized through various interaction metaphors such as 3D sketching, deformation and puzzles. The creation and rearrangement of cardiovascular structures by learners in a virtual space is beneficial to the spatial understanding of complex anatomy and can be realized through various interaction metaphors such as 3D sketching [35, 36], deformation and puzzles [33].

2.2 Embryology Teaching & Visualization

Visualizing The Developing Brain[1] is a project of the Center of Anatomy and Human Identification at the University of Dundee to help students better understand the morphological development process and in particular the difficult-to-visualize 3D folding of the early human brain. An interactive animation video and 3D model show the growth of the embryo and, in particular, the brain and its individual components.

There is a wide variety of approaches ranging from physical models of embryonic organ systems or cardiac malformations, created using 3D printing techniques to match the teaching content, in comparison to conventional media and 3D digital representations [9, 40]. Bakker et al. [12] realized a 3D atlas of human development that depicts the temporal development of all organ systems. This atlas allows students to explore different embryo structures using a PDF file with interactive 3D models. This tool lacks in the performance to be used fluently: while it depicts the different stages, it does not show the transition from one stage to another. Hull et al. [20] evaluated the use of a visualization of craniocaudal folding at the beginning of embryogenesis, which represented three time points of development. Buttons could be used to switch between the stages, which were displayed on screen using classical 3D viewers. Individual organ systems could be faded in and out individually. Even though the application provides an interactive understanding of temporal folding formation, this approach lacked the substantial immersion which could be provided by Mixed Reality Approaches. Gustilo et al. [17] developed an interactive mobile application called Embryonic Virtual Heart Application (EVHA) that contains a series of anatomical 3D models of the embryonic heart with and without congenital heart defects which already shows that the students benefit from a 3D Model. Further indications of the general usefulness of an immersive concept were presented by Tait et al. [42] who used a 3D reconstruction of sheep embryos in conjunction with images of the corresponding histological slides, which could be viewed in a mobile application for Android tablets in a classic 3D viewer and in handheld AR. The results of the evaluation suggested that the use of a 3D modality such as the presented AR application significantly improves the understanding of slide alignment compared to current methods. In addition, the application was considered more interesting, useful, and user-friendly than current histology tools.

In the area of integrating new visualization approaches into the curricula in use, two works are particularly noteworthy. First, a case study where Meguid et al. [1] describe how they integrated the Human Developmental Biology Resource (HDBR) atlas[2] and the 3D Atlas of Human Embryology[3] into the curriculum at Newcastle University and provide a perspective on how these new learning resources might impact teaching in the future. The HDBR atlas is a database of embryological tissue samples from human embryos donated to research for educational use and includes rendered animations of rotating organs, 3D models of segmented organ systems, and histological embryo sections [16]. Second, Moraes et al. [2] provided students with multimedia materials of embryos, e.g., clinical histories, autopsy images, ultrasound images, movies, and animations. The teaching material was used by the students in class and subsequently accompanied by a knowledge examination and interviews. The multimodal use proved to be useful and was able to reveal knowledge gaps between basic sciences and clinical disciplines for medical students. This demonstrates the potential of a multimodal, immersive learning experience for teaching such a difficult topic. We decided to complement the existing approaches with a study in a VRLE to expand the possible interactions with the topic.

3 Material & Methods

In this section, we present the process of developing our VRLE based on user research. In doing so, we address the context of use and highlight the requirements. Finally, we present the resulting prototype, user interactions, and technical details, and define our goals in terms of a learning scenario.

[1] https://visualisingthedevelopingbrain.co.uk
[2] https://hdbratlas.org/
[3] https://www.3dembryoatlas.com

3.1 User Research

The basis for user-centered design is the determination of user needs through the analysis of the environment, ergonomic aspects as well as specific problems. On the basis of three semi-structured expert interviews with lecturers and physicians from the medical faculty of our University (Institute of Anatomy and Clinic for Cardiology and Angiology, University of Magdeburg), requirements for teaching and learning were identified, which were used to design a prototype with a suitable interaction concept. Similarly, we conducted a survey of medical students to determine which sections in cardiac development are difficult to understand. After analyzing the current teaching situation at our university and identifying the challenges faced by students, an interdisciplinary team of software developers, designers, and medical professionals developed ideas and approaches for technical implementation based on the requirements.

3.2 Context of Use

Anatomy education aims to provide medical students with an understanding of the morphology and function of anatomical structures, their location and spatial relationships, and is an important prerequisite for understanding diseases and their treatment [32]. Traditionally, anatomy education includes lectures, use of textbooks and atlases, and dissection of human bodies provided by donors [31]. The dissection course, in particular, is essential because it is an active way of learning that exercises topographical knowledge and manual dexterity. Furthermore, it allows the students to understand the connections between the anatomical structures [7].

The term embryo refers to the first developmental stages from fertilization to the end of the eighth week of pregnancy (day 56). The cardiovascular system is the first functional system of the embryo. The heartbeat can be detected by ultrasound as early as the 4th week of development. The development of the heart (cardiogenesis) can be roughly divided into two stages: Formation of the cardiac loop (1) and formation of the interior of the heart (2).

At our university, embryology is taught in the first year of training in the course of human medicine, both in the form of lectures and as a seminar in the dissection course. In the lecture, images and videos from various sources are used and reference is made to further sources on the intranet or literature for self-study. The embryology of the heart is taught in small groups of 5-10 people during a half-hour breakout session in a dissection room. The survey of medical students revealed that the formation of the primary heart tube and cardiac looping were considered particularly difficult. In teaching embryology knowledge, two aspects are especially important for interviewed lecturers:

1. Understanding complex, time-dependent, 3D morphological changes in the developing embryo.
2. Attention to the clinical implications of congenital organ defects that arise when these morphological processes deviate from the norm.

3.3 Concept

For the concept reported in this article, the focus was on aspect 1; the spatial understanding of shape transformation. Since the formation of the heart loop involves a 3D overlay, this development is difficult to understand in two dimensions. As a result, instructors have established a method of using different colored modeling clay to simplify the fusion into the primitive heart tube and subsequent loop formation (see Fig. 2). At the same time, this method also conveys the changing positional relationships after each step of the formation. Inspired by this practice, the advantages of VR were used so that the shape change can be displayed immersively. The resulting 4D concept, unlike existing static models, is intended to animate shape and position changes in temporal transitions between development stages, making it an interactive experience. The video attached in the supplementary material illustrates the concept created.

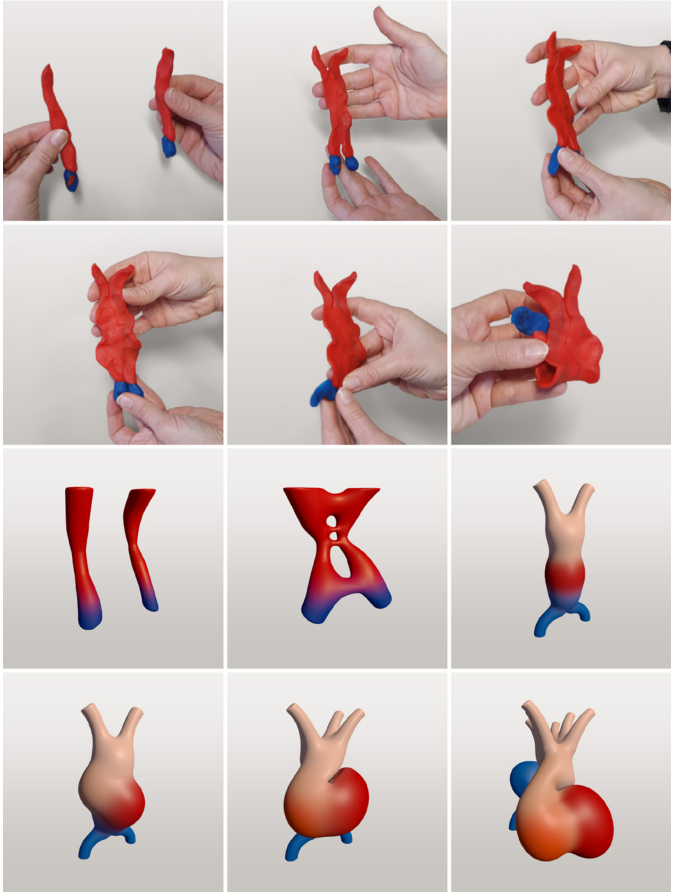

Fig. 2: Comparison view of the real and virtual contents of the three phases of heart development implemented in the VRLE. Top: Modeling clay used in class. Bottom: Derived virtual 3D models.

3.4 Virtual Learning Environment

Based on the previously described concept and in constant exchange with cardiologists, we have developed a virtual learning application in an iterative design process with a focus on interactive visualization of learning the temporal evolution of the human heart.

We propose a virtual seminar room where users can explore the development of the heart and manipulate the transitions with hand interactions. Here, deformable 3D models of the early heart can be explored at different stages to promote spatial understanding of the development. Three phases of early heart development have been implemented:

1. Formation of the primitive heart tube (day 20 - 21)
2. Formation of the cardiac loop (day 22 - 23)
3. Completion of the S-shaped heart loop (day 24 - 35)

3.4.1 Interactive Modes

In addition to the 3D models of the different stages of the heart, the environment includes four modes. The first mode, *Training Mode*, is designed to familiarize the user with the interaction techniques in VR; in particular, it allows inexperienced students to get started easily. Here, the user is presented with basic 2D and 3D elements such as sliders, buttons, and toggle switches. The second mode, *Exploration Mode*, shows segmented 3D models of corresponding embryos. In addition to the isolated heart, other anatomical structures and organs can be faded in and out to visualize the context. The central element is the third mode, *Learning Mode*, which is intended as training unit to interactively simulate 4D morphological development and to promote spatial understanding. Supporting this, 2D diagrams with cues and labels are

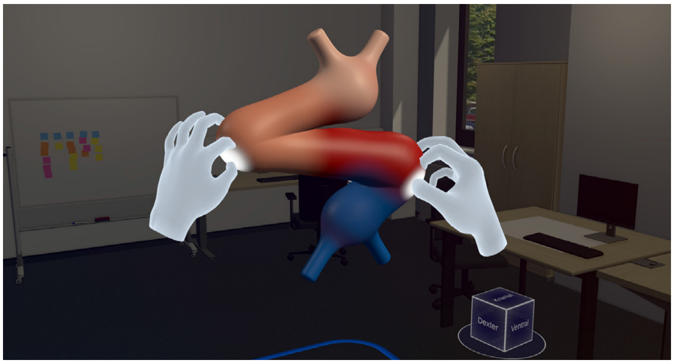

Fig. 3: Modelling mode allows the user to deform the heart tube freely and without restrictions.

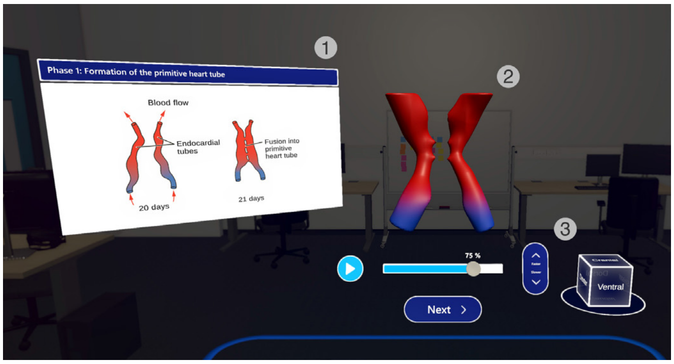

Fig. 4: VRLE in *Learning Mode* with passive features. (1) 2D graphical scheme with descriptions, (2) 3D model in current transition, (3) UI elements for manipulating the animation: buttons, slider and navigation cube (right).

provided, as well as various interaction elements to manipulate the heart model. An overview of the *Learning Mode* is shown in Fig. 4. A final fourth mode, *Modelling Mode*, has been implemented to allow free modeling of a heart tube (see Fig. 3).

3.4.2 User Interface

To get from the initial state (A) to the final state (B) of the morphological change within a development step, the user has several tools at their disposal, which can be seen in Fig. 4. On the user's left side in the virtual environment, there is an illustration[4] describing the current development stage. The two states (A + B) are marked with the respective day in the development, as well as labels of the anatomy. In the center, below the 3D model, is a playback control (play | pause | toggle) that activates the change as an animated motion. Parallel to this, a progress bar shows the current stage of the development over time in percent (0 - 100) and can also be continuously changed directly by the user with his hands on the handle. Furthermore, it is possible to adjust the playback speed of the animation in discrete steps via a toggle switch. The animation can be stopped at any point. This gives the user time to scale, rotate or move around the 3D model. The 3D models can be rotated and scaled via a widget, a so-called navigation cube that displays the anatomical position. Rotation is restricted to the cranial axis. The scaling is unlimited. When multiple 3D models are displayed, the manipulation of this cube affects all 3D models synchronously. A button takes the user to the next of the three development stages. To strengthen the focus on the learning content, the entire user interface (UI) is separated from the environment. Thus, the environment appears darker and attracts less attention because a semi-transparent box is placed around the user and the controls are located in a recessed area.

3.4.3 Hand Interaction

To make the interaction as natural as possible, users can deform the model and corresponding structures with their hands. To do this, the user grabs the virtual heart with both hands at the points marked with a cross. Learners benefit from the provision of additional navigational aids for guided exploration in VR, which is why we emphasized feasible interaction on the 3D model [10]. Two black and white dashed arrows on the virtual heart indicate which movement has to be executed to transform the object from one state to the next (see Fig. 1).

Analogous to the animation, only a linear deformation can be performed. Thus, a free interaction is imitated by a guided movement, which prevents unwanted deformations and makes the real physiological development comprehensible. The interaction must be bi-manual, since each hand is intended to imitate a part of the complex movement at certain points of the model, and these processes also run in parallel in reality. This guided linear control of the interaction was chosen because it corresponds to physiological development. As described above, we implemented a fourth mode for free deformation. This is an experimental function that has no restriction on the degrees of freedom and allows the user to perform any kind of virtual shaping.

3.4.4 Active and Passive Features

Although active interaction with 3D models in a virtual environment leads to a more efficient viewing of objects [21], this does not take into account individual learning types. For this reason, we implemented two features with different interaction modalities to address individual learning types of the target group and to investigate the advantages and disadvantages of these features. Thus, the *Learning Mode* can be performed in both a passive-explicit and an active-implicit variant. The difference lies in the UI: in passive training, the user has the classic UI elements such as buttons and sliders to control the animation. In active training, the layout is identical, but the playback control buttons are hidden and it is not possible to interact with the progress bar. For manipulation, the user only has direct interaction with their hand on the 3D model. When the task is completed in the active training, the animation can be reset or played back using a button.

3.4.5 Technical Setup

Software development was done using Unity 2020.3.35f1[5] in C# on Microsoft Windows 10 Pro (build 19044). Microsoft's Mixed Reality Toolkit (MRTK) for Unity[6] (v2.7.2) was used to integrate hand tracking using Ultraleap[7] Hand Tracking v5.2.0 and Leap Motion Core Unity Plugin[8] v4.9.1 packages. MRTK interface building blocks were utilized to design the UI.

The interactive models of the embryonic heart were created with MudBun[9] v1.3.29. This tool employs signed distance fields for procedural volumetric mesh generation, which allows for real-time modelling of organic shapes directly in the Unity editor and in the built application at run-time. For polygonizing the 3D scalar field several meshing algorithms were tested. Marching cubes provided the best results while maintaining a high frame rate. Spatial hashing and sparse voxel trees are utilized to achieve acceptable performance (circa 90 FPS) for VR.

On the hardware side, the prototype was realized using Valve Index VR glasses (Valve Corp., USA). The HMD was extended at the front with Ultraleap's Stereo IR 170 Evaluation Kit (Ultraleap Ltd.) hand tracking sensor by a 3D printed mount to enable touchless interaction. The hardware specifications of the used PC were: Intel Core i7-9700 3GHz 8-core CPU, NVIDIA GeForce RTX 2080 Ti, 32 GB RAM, 512 GB PCIE 3.0 SSD.

[4]Used under CC BY 4.0: https://openstax.org/books/anatomy-and-physiology/pages/19-5-development-of-the-heart

[5]https://unity.com

[6]https://learn.microsoft.com/windows/mixed-reality/mrtk-unity

[7]https://www.ultraleap.com

[8]https://developer.leapmotion.com/unity

[9]http://longbunnylabs.com/mudbun

3.5 Learning Objectives

Our VRLE is designed to allow students to explore theoretical knowledge about the development of the early human heart in an exploratory manner based on a problem-based learning approach [19]. Thus, it should be possible for students to use this VR application in self-study, e.g. after the initial lectures on the topic of heart development. The VRLE is designed as a controlled environment in which users can focus on the essential learning content without external influences. The learning experience is motivated by a sense of embodiment [28], focusing on natural hand interactions. This is because it was also evident from the literature and interviews that learning with the hands through palpation of the organs provides an advantage in terms of spatial understanding and positional relationship. Likewise, the goal was to accommodate different learning styles [27], so we want to enable active and passive learning of 3D objects [22] through different features and provide guided exploration with a appropriate didactic design [10].

4 Evaluation

To address different types of learners and to explore the potential learning context, we implemented different functionalities in our prototype to explore the early human heart and integrated them into a virtual learning environment. We evaluated this environment in terms of usability, perceived task load, and sense of presence using quantitative measurements and qualitative feedback from the potential target audience: medical students. We also determined spatial awareness and knowledge gain using a self-developed test. Furthermore, we presented the prototype to a group of non-medical professionals with technical backgrounds and predominantly high affinity for VR to assess the quality of the VRLE in terms of usability and presence for non-domain experts. The technical group was not asked about the medical quality of our VRLE. Finally, we presented the application to three domain experts: two practicing cardiologists and an anatomy lecturer who were not involved in the development of the VRLE. In this way, we received feedback on our test, advice on the appropriateness of the use scenarios, and guidance on how to incorporate our VRLE into a future curriculum. Our evaluation, based primarily on the collection of qualitative data, thus takes an exploratory approach, which allows the application to be improved through feedback from various stakeholders.

4.1 Study Design

We divided the group of medical students into two test groups, with group Active (A) starting the experiment with the active feature as the first condition and group Passive (P) starting with the passive feature in *Learning Mode*. Since modes 2 - 4 are our central learning tools, our investigation focuses primarily on these elements within the application. Usability and presence of our VRLE was evaluated using the System Usability Scale (SUS) [8] and Igroup Presence Questionnaire (IPQ) [38]. The IPQ includes three subscales and a fourth general item (sense of being there), which are considered in our study: *Spatial Presence* (SP), *Involvement* (INV), *Experienced Realism* (REAL) and *General* (G). As an indicator of subjective perception and task load of our interaction concepts, we analyzed the overall unweighted NASA TLX score (Raw-TLX) [18]. Based on the Think Aloud protocol [41], participants were asked to express their thoughts while interacting with the VRLE. In addition, we conducted a semi-structured interview at the end of the experimental series.

4.1.1 Mental Rotation Test

Spatial understanding and mental rotational ability are predictors of intelligence and are therefore often used as tools in the medical school application process. To elicit rotational ability within our sample, we used the *Mental Rotation Test (MRT)* in the variant of Ganis and Kievit [15], as it has 3D views and allows for better assignment of positional orientation in space through improvements in terms of shading and depth perception. The mental rotation test consists of 96 pairs of cube figures, each of which must be decided within 7 seconds whether they are identical or different. At the beginning there is an instructional text and 10 sample items. The test takes about 10 minutes.

4.1.2 Custom Anatomy Knowledge Test

In order to find an indicator of knowledge transfer for our VRLE and its use as a learning tool, we developed an anatomy knowledge test (AKT) consisting of 30 questions (see supplementary material). We divided the test into three categories with a different set of questions critical to understanding cardiac development. In the *Shape* category (15 questions), the participant had to identify illustrations that did not match the anatomical structures from the training phase. The discrepancies were created by mirroring, leaving out, or distorting sections. In the *Time* category (4 questions), the participant had to place 6 illustrations in the correct chronological order. In the last category, *Location* (11 questions), the participant had to identify a cube (analogous to the navigation cube from the VR application) from 4 possible variants that matched the illustration shown. Each category had questions with colored and colorless images.

4.2 Participants

To evaluate our two implemented modes, we recruited 19 participants with medical and technical background. Twelve medical students (8 women), aged 24-30 years (Median (Mdn) = 27) were recruited from our university, each compensated with 20 euros per hour. All participants had already taken anatomy courses, with 11 participants between their 6th and 15th semesters of study (Mdn = 10) and one graduate student included. Seven individuals reported having corrected visual impairments. A rating scale from 1 (no experience) to 5 (very experienced) was used to rate the following: technical affinity (Mdn = 3), VR experience (Mdn = 2), gaming experience (Mdn = 2.5), prior knowledge of embryology (Mdn = 2.5). Three participants reported having no VR experience. None of the participant reported color vision deficiency. Most participants indicated that their last contact with embryology was a few years ago.

The second group of non-medical students with technical background aged 22-30 years (Mdn = 27.5) included 7 unpaid participants (3 female) from our university. Here, four participants reported having corrected visual impairment. We used the same rating scale and obtained the following ratings: technical affinity (Mdn = 4), VR experience (Mdn = 3), gaming experience (Mdn = 4), prior knowledge of embryology (Mdn = 1). Five participants rated their technology affinity as 4 or higher. One participant reported having no VR experience.

4.3 Setup

The study took place in a 70 m^2 VR lab at our university. One participant and one investigator were in this room during each of the data collection sessions. For the participant, there was a separate seat with monitor, keyboard and VR headset next to the experimenter's recording seat. Inspired by Voit et al. [43] who, among other surveys, investigated the user experience and presence in a physical in-situ and a virtual lab environment and reported comparable results regarding user insights and feedback, we created a virtual replica of our laboratory. This safe and controlled environment is intended to serve as an orientation for the users in the real world and is to be understood as a proxy of a seminar room. The virtual room in which users could move around had an area of approximately 3 m × 4 m and was marked by a virtual blue line.

4.4 Ethics Approval & Hygiene Policy

The experiment was conducted during the global SARS-CoV-2 pandemic. Therefore, a strict hygiene policy was followed. Specific ethics approval was not required by our institution. The occupational safety and health department approved all relevant measures.

4.5 Procedure

The user study took approximately 90 minutes. At the beginning, all participants were informed about the data protection, hygiene regulations, and the procedure of the study. The collection of demographic data was followed by the mental rotation test on the participant's screen using keyboard input. The content of the screen was mirrored on the monitor of the investigator. This test lasted about 10 minutes. After the test participant entered a marked area in the center of the tracking space, the VR headset was put on and individually adjusted, followed

Table 1: Summary of descriptive results. All entities are in the format: mean value ± standard deviation (median).

Variable	AKT	Raw-TLX	SUS
Active	0.63 ± 0.17 (0.68)	17.15 ± 11.42 (13.30)	90.00 ± 9.19 (92.00)
Technical	0.54 ± 0.26 (0.50)	13.21 ± 6.51 (10.80)	94.86 ± 4.14 (96.00)
Medical	0.68 ± 0.11 (0.71)	19.44 ± 13.22 (16.65)	87.17 ± 10.25 (89.00)
Passive	0.74 ± 0.05 (0.72)	12.89 ± 9.50 (10.00)	92.74 ± 5.59 (94.00)
Technical	0.74 ± 0.05 (0.73)	9.16 ± 5.78 (8.30)	95.43 ± 3.95 (94.00)
Medical	0.74 ± 0.05 (0.72)	15.07 ± 10.74 (11.25)	91.17 ± 5.94 (93.00)
First Training	-	14.99 ± 10.40 (10.80)	90.32 ± 8.88 (92.00)
Active	-	18.42 ± 10.17 (15.80)	87.56 ± 11.26 (90.00)
Passive	-	11.91 ± 10.10 (8.30)	92.80 ± 5.51 (94.00)
Second Training	-	15.05 ± 11.05 (11.70)	92.42 ± 6.20 (94.00)
Active	-	16.00 ± 12.88 (12.05)	92.20 ± 6.70 (95.00)
Passive	-	13.99 ± 9.26 (11.70)	92.67 ± 6.00 (94.00)

by a short introduction to the virtual environment. A reading test with small text in VR was performed to assess visual performance. The participant was now in the virtual lab and first saw a tutorial consisting of building block elements of the MRTK framework (*Training Mode*). By interacting with 2D and 3D interfaces such as sliders and buttons, the participant was to familiarize him or herself with the functions of hand tracking.After familiarizing themselves with the interactions, a button took them to the *Exploration Mode*, where they could examine the different developmental stages of the embryos and, primarily, their cardiovascular system. With a start button, they then initialized the central *Learning Mode*. The test groups A and P then first started the VRLE with the respective assigned variant of the *Learning Mode* and were asked to comment on their activities. The task was to move the virtual object from the initial state (A) to the final state (B) by a given interaction. If 100 % of the required movement was performed, the task was solved. A green check mark and an audio signal indicated the correct solution of the task. After that, the operation was the same as in the passive variant, except that there was an additional button to reset the interactive task. The Next button could then be used to jump to the next stage of the development. Upon completion of the initial training phase, the participant was asked to complete the NASA TLX and SUS questionnaires and take the AKT. Afterwards, the training was repeated with the respective other variant. This was followed by the completion of the questionnaires and the repetition of the AKT in a second variant, whereby the same tasks were presented in a different order. The experimental *Modelling Mode* for free-form deformation could be explored. Upon completion of all phases of training, the IPQ was completed and data collection ended with a final semi-structured interview that allowed participants to provide feedback on the VRLE experience.

4.6 Deviations from the Protocol

We used the same methods and procedures to collect data from participants with technical background. Because of the lack of medical qualifications of this group, the focus of data analysis was on the technical aspects of the VRLE. Therefore, we did not collect qualitative feedback or analyze this data. The three experts who were asked to be interviewed did not go through the study design but were asked to examine the application and its function exploratively and to describe their impressions. The experts' statements were then discussed, documented and evaluated. We interpreted the experts' opinions as feedback to rank the suitability of our VRLE in the educational context.

4.7 Data Analysis

We summarized the individual statements of study participants with medical backgrounds into specific categories in tabular form. The categories included statements about the UI, interaction with the 3D models, cardiac development, anatomical knowledge, and the VRLE in general. For the descriptive analyses, mean values and medians were calculated for all measured variables. There, we differentiated between participants of the technical and the medical domains. Regarding the MRT, the error rate (number of errors divided by total number of items) was multiplied with the average response time for each participant to obtain a single mental rotation measure, with a lower score indicating better performance. Finally, post-hoc analyses were conducted to analyze the correlation between performance and mental rotation capabilities.

5 Results

The primary goal of the evaluation was to examine the usability and presence of our VRLE. The results should give us indications for the assessment of the implemented functions and the active and passive interactions. Therefore, the division into two groups was made. In the second step, we used this subdivision to analyze these groups in their learning behavior, since the long-term goal is to be able to provide a learning platform. To this end we examined cognitive aspects through the mental rotation and the anatomy knowledge test. In this section, a descriptive analyses on measured data is presented. In addition, final interview and expert interview results are reported.

5.1 Descriptive Analyses

We performed a descriptive analysis of the data with respect to the background of the study participants. The summarized results are shown in Table 1 and are visualized in Fig. 5. Regarding the AKT, no major differences were found between the user groups. Participants with a medical background performed similar with both, the active (*average* $(avg) = 0.68$, *standard deviation* $(sd) = 0.11$) and passive ($avg = 0.74$, $sd = 0.05$) features. Participants with technical backgrounds achieved, on average, noticeably lower scores compared to the other test group when using the active feature ($avg = 0.54$, $sd = 0.26$). However, they showed similar AKT scores with the passive feature compared to the medical group ($avg = 0.74$, $sd = 0.05$). Overall, the VRLE achieved low task load scores on Raw-TLX questionnaires ($avg = 15.02$, $sd = 10.58$). In the mean, the medical student group rated the VRLE as more demanding ($avg = 17.26$, $sd = 11.99$) compared to the technical group ($avg = 11.19$, $sd = 6.28$). On average, the passive feature was assigned a lower task load ($avg = 12.89$, $sd = 9.50$) and higher usability ($avg = 92.74$, $sd = 5.59$) than the active one (Raw-TLX: $avg = 17.15$, $sd = 13.30$; SUS: $avg = 90.00$, $sd = 9.19$). The SUS questionnaire data consistently showed high scores ($avg = 91.37$, $sd = 7.63$) for the VRLE among all user groups, features, and training phases, with the technical background group showing the higher usability ratings ($avg = 95.14$, $sd = 3.90$) compared to the medical group ($avg = 89.17$, $sd = 8.44$). Concerning the IPQ questionnaire data (see Fig. 6), high scores in the areas of General ($avg = 4.21$, $sd = 0.64$) and Spatial Presence ($avg = 4.88$, $sd = 0.64$) are observable. In contrast, Involvement ($avg = 2.97$, $sd = 1.06$) and Experienced Realism ($avg = 2.89$, $sd = 0.74$) received the lower overall scores. Users with technical background consistently reported higher scores compared to the medical group (Technical vs. Medical: G $avg = 4.71$, $sd = 0.47$ vs. $avg = 3.91$, $sd = 1.14$; SP $avg = 5.00$, $sd = 0.50$ vs. $avg = 4.82$, $sd = 0.71$; INV $avg = 3.52$, $sd = 1.05$ vs. $avg = 2.64$, $sd = 0.94$; REAL $avg = 3.01$, $sd = 0.77$ vs. $avg = 2.82$, $sd = 0.72$).

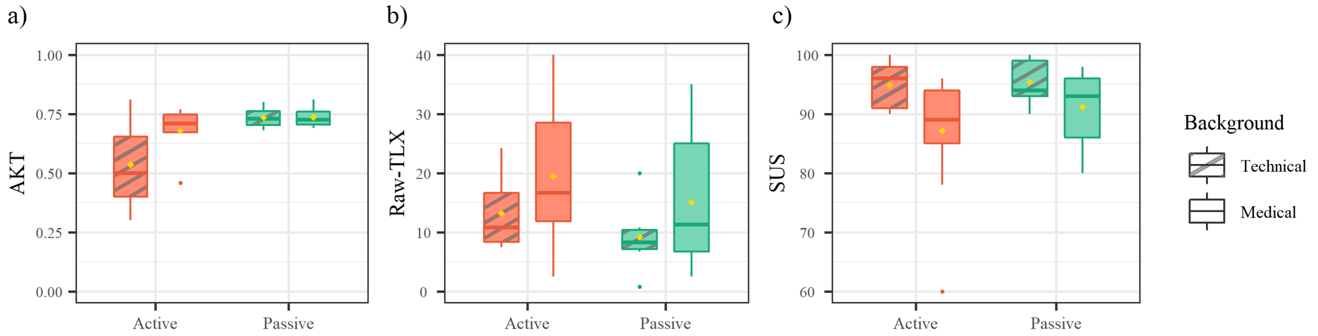

Fig. 5: Descriptive results of active and passive features on AKT, Raw-TLX and SUS scores with respect to participant background. Yellow diamonds indicate mean values. The scales of the Raw-TLX and SUS scores were truncated after 40 (max. 100) and before 60 (min. 0) respectively for better visibility of differences.

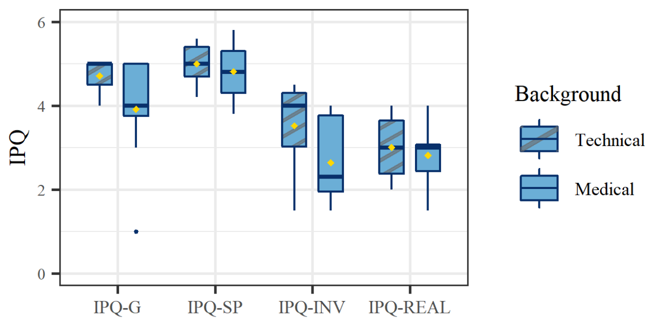

Fig. 6: Descriptive IPQ results with respect to participant background. Yellow diamonds indicate mean values.

Table 2: Summary of MRT Pearson correlation test results ($\alpha < .05$)

Training / Variable	df	p	r	Cor.
Complete Data				
AKT	17	0.006	-0.601	*
Raw-TLX	17	0.122	0.367	
SUS	17	0.179	-0.322	
IPQ-G	17	0.587	-0.133	
IPQ-SP	17	0.539	-0.150	
IPQ-INV	17	0.905	0.029	
IPQ-REAL	17	0.077	0.416	
First Training				
Raw-TLX	17	0.007	0.593	*
SUS	17	0.011	-0.569	*
Second Training				
Raw-TLX	17	0.733	0.084	
SUS	17	0.479	0.173	

5.2 Post-Hoc Analyses

We were interested in whether mental rotation capabilities correlated with performance outcomes. Therefore, we conducted post-hoc Pearson correlation tests between the MRT results and all other acquired questionnaire data. Results are reported in Table 2. No significant correlation effects were detected except for the AKT. It appeared that, worse performance in the MRT also resulted in worse AKT results. This effect is illustrated in Fig. 8.

In addition, a secondary review of the raw data revealed differences between the first and the second training runs of participants. To this end, we conducted separate descriptive analyses of the individual training sessions (see Fig. 7). Raw-TLX ratings in active and passive features showed similar results in the second training. The active feature seems to have a higher task load in the first training compared to in the second one. As for the SUS score, we see similar results in both sessions in terms of the passive feature. The active feature achieved higher scores in the second training. Separate Pearson correlation tests were performed between MRT and both questionnaires for results of the first and the second training individually. Results of these tests are included in Table 2. No correlation was found regarding the second training. However, the Raw-TLX and SUS scores of the first training significantly correlated with the MRT results.

5.3 Final Interview Results

We transcribed the audio recordings from the final interviews with medical students into collected transcripts, resulting in a total of 195 individual statements. We summarized 86 statements and assigned them to five categories. Only statements that were consistent among at least three participants were included. This summary is presented in Table 3.

5.4 Feedback from Domain Experts

In this section, we provide a summary of expert feedback obtained through the demonstration of our VRLE and subsequent interviews. In general, the experts rate our VRLE very positively. The advantages of the 3D interaction are particularly emphasized, because the intuitive merging makes the physiological deformation understandable and simply fun. It resembles manual dissection on the adult heart and thus promotes spatial relationship and context. The limitation that the model cannot be viewed from all body axes was criticized, which makes folding in the lower area as well as looking inside impossible. This could be remedied by a mode change button that distinguishes whether one wants to deform or rotate the model.

Free modeling is seen more as a creative feature for tracing. Students would have too many degrees of freedom, which stimulates the play instinct, but is too time-consuming. Also, it does not reflect physiological development. One could restrict the movements by surrounding the heart tube with an adjacent pericardium.

The active feature was unanimously positively received, even if it was more difficult to handle at the beginning, as it stimulates motivation and can thus promote longer learning. With regard to the passive function, it was noted that one is less distracted and can thus pay more attention to details.

Since much emphasis is placed on technical terms in medical education, these terms should be constantly visible and correctly assigned. Although our 2D display provides information about (development) day and stage as well as the designation of the anatomical structures, medical terms should be displayed directly in the dynamic development process at the respective structures. Furthermore, it should be possible to show and hide these annotations so that learners can query the knowledge about the terms.

Visualization of the heart meets the requirements in terms of color

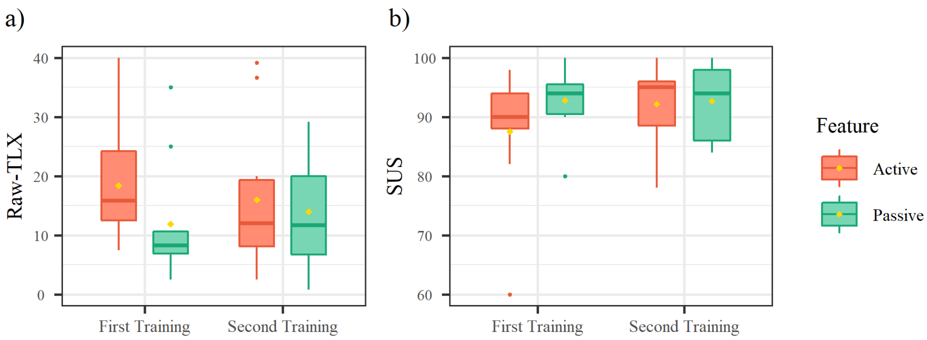

Fig. 7: Descriptive results of the individual first and second training on Raw-TLX and SUS scores with respect to the features tested in that training. Yellow diamonds indicate mean values. The scales of the Raw-TLX and SUS scores were truncated after 40 (max. 100) and before 60 (min. 0) respectively for better visibility of differences.

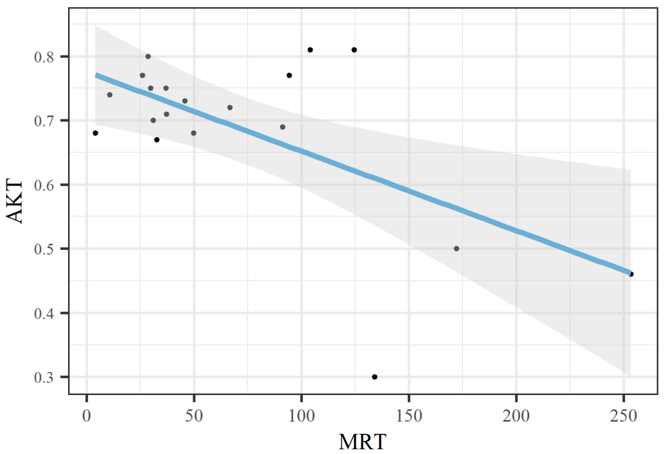

Fig. 8: Correlation between MRT and AKT results

Table 3: Summary and number of statements (#) sorted by category (left) from the medical student survey.

3D Interactions	Trouble rotating the cube as intended (7) Rotation around other axis desired (tilting) (5) Connection of cube and model rotation is intuitive (4) Walking around is easier than rotating via cube (3) Two-handed rotation is easier than just one-handed (3) Setting down the cube for larger rotations is awkward (3) Rotation takes time to master and requires practice (3) Desire to rotate the model directly by touching it (3)
Active	Multiple attempts required to successfully trigger two-handed interaction (5) Difficulty with hand tracking, coordination problems (3) Trouble performing the two-handed grab and transform (3) Better than passively watching the animation (3)
Passive	Calm viewing experience improves perception of details (4) Ability to precisely control the speed is rated positively (3)
Free-form	Option to add more details is desired or expected (5) Greater creative freedom is positive for learning success (4) The level of detail of the modeling is more imprecise than guided interaction (3)
General	Complexity and costs of VR are viewed as disadvantages (3) Desire for an audio guide that leads through the content (3) Annotations of anatomical structures should be displayed as an option (3) More content needed for better chronological context (3) 3D representation is superior to classic illustrations from textbooks (3)

and shape, so no need for more realism is seen. It was criticized that the overall context of the heart in relation to the embryo is missing. The embryo and its surrounding structures should be able to fade in and out, with attention to color coding. Approval was also given to the simplicity of the environment, as there are no distracting visual and auditory elements.

Our custom AKT was rated as very demanding. However, the experts were not sure whether logical thinking or actual knowledge is required here. The "Time" category, for example, is very easy to solve. No difference could be found between abstract shapes and anatomical structures.

The application receives majority approval because it promotes 3D understanding and is didactically well prepared. Although it shows only a small part of the development and hides internal changes, it gives a clear insight into the complex development of the heart. For possible integration into the learning process and the later curriculum, individual training is being considered, with a detailed auditory explanation to guide the user.

6 Discussion

The addition of a group with a technical background served us primarily to survey the usability of the VRLE. This group rated our application slightly higher overall in terms of the given measurement tools, which can be attributed to their familiarity with VR applications. However, it turned out that not only technically skilled users rated the application as very usable overall. Our application was certified as having an overall very high level of usability with an average SUS rating of over 90 [5]. We speculate that the slightly lower rating of physicians is due to unfamiliarity with VR applications in the context of varying familiarity with VRLE. This may be due to the fact that our VRLE has a reduced interface and is relatively small in scope. Nevertheless, the given elements seem to satisfy the requirements of users and experts for the given use case. Due to our small sample size and the chosen study design, we were unable to demonstrate that our VRLE influenced learning outcomes. However, there is recent work indicating improved learning success in anatomy education through immersive VR [26], which again is consistent with the expert opinion in our work. Related work in the area of embryology teaching [9, 12, 17, 20, 42] covers more developmental phases in snapshots. We distinguish our work by visualizing the morphological transitions within each phase, albeit fewer, interactively for students. According to our sample, the high IPQ score shows that our VRLE induces presence. In particular, the high scores in the sub-scales "General Presence" and "Spatial Presence" show that users felt present in the VRLE and were able to interact without being disturbed. The lower scores for "Immersion" and "Realism" are due to the fact that the interactive models are abstract visualizations rather than real organs. There are no clear differences between both user groups in usability ratings of the application, but there are clear differences in subjective task load and IPQ, which could indicate cognitive overload. It is also clear from the feedback of the participants that some types of learners are more likely to benefit from passive use of the VRLE. For example, an animated 3D display that can be scaled and viewed at rest may provide an advantage as users are less distracted. The passive feature has a low subjective task load, which is due to the fact that users perform few movements and generally interact less. Therefore, the overall task load is lower.

Jang et al. [23], found that passive viewing, as opposed to interactive direct manipulation in 3D structures in a VR environment, was less effective for learning in anatomy education. In our active variant, the members of the technical group perform the AKT poorly. This could be attributed to the small sample, but could also indicate a better learning experience in the passive environment. Also, it should be noted that the test is not targeted at this group. Since we are using this study as a pilot for more extensive testing and evaluation as part of the curriculum at our university, we are looking for evidence of differences in learning styles. Lee et al. [27] demonstrated that VRLEs can accommodate learners with individual learning styles.

The statements of the experts and medical students as well as their data show that the AKT probably asks for logical thinking rather than (learned) anatomical knowledge. Accordingly, it could rather be considered as a reduced version of an MRT, since the task design of both tests is very similar. This could also explain the significant correlation effect between both test results. The MRT correlation tests between first and second training, may indicate that the accumulated experience in previous study runs, positively affects the training afterwards.

As VR technology becomes more commonly used in medical education, the differences in performance between users in our tests may become less noticeable over time. Multi-user learning environments [37, 44] for anatomy teaching play a major role in the literature as they can promote collaborative exchanges between students and teachers and support the understanding of anatomical structures through a high degree of immersion [29]. We have opted for a protected space where a single user can focus on the learning content. However, we see our application as transferable to a seminar environment where the instructor can participate in the VRLE as a facilitator or take on the role of active demonstrator themselves.

7 Limitations

The implemented features "active" and "passive" differ only slightly in the actual interaction of the user. The only difference is where users can place their hands, after which a controllable animation is played. The possibility of rotating the models or the interface element also leads to a difficult differentiation. The sample selected for our evaluation has an above-average mental rotation ability compared to the validation sample of the test of Ganis and Kievit [15], which could lead to users with lower abilities performing worse. Our tested groups are not balanced and the sample is generally too small for our secondary questions. Due to this small sample, we see no evidence of possible significance, which is why no further statistical analyses (e.g. ANOVAs) were performed. The possibility of free modeling of the heart tube appeared tempting in terms of interactivity and the associated playful increase in user motivation, but proved to be unsuitable because this does not reflect physiological development and thus contributes little to learning success. However, in this case, the pericardial limitation could provide guidance or restriction to the user, so this may be a compromise between free movement and real development. While our visualization meets the requirements, it does not allow for an inside view of inner structures. Although we depict smooth transitions within a phase, we do not provide the possibility of a seamless transition. The developed AKT contains only images of the own visualization and is therefore not representative for anatomical representations analogous to literature or real tests. In addition, the participants went through the same test twice - but with different order of questions.

8 Future Work

Ongoing work should include selectable options with passive and active features to address different learning styles. In this way, the user can select the setting that suits them best and, after a certain period of familiarization, the overall experience can be increased. Our VRLE is limited to the development of the heart only, but offers the possibility of adaptation to other similarly complex processes, such as the formation of the inguinal canal or the pharyngal arches. Since the availability of VR technology in medical education is still limited, AR approaches (e.g. handheld devices could expand the potential user group. We deliberately used a virtual replica of our examination room to provide users with a familiar but interchangeable environment. Accordingly, it is easy to adapt a learning scenario with AR glasses analogous to our setting, which would allow further collaborative learning approaches and direct integration into the dissection course to be pursued through physical presence. Despite the great enthusiasm for such technologies, future work should be careful to create fractures to enable equity by overcoming barriers such as device deployment and individual student needs [24].

Moreover, the importance of learning medical terms should not be underestimated, with annotations directly on the object playing a major role. Our application also lacks the ability to display proportions and interior views. The most elegant idea would be to first model the organ from the outside and then slice it open to show the septation inside, illustrating parallel development. Also, parallel cardiac defects could be shown on a timeline as a function of phase to illustrate clinical relevance and thus be used by trainee cardiologists.

We developed the requirements for this application from user research and, in particular, from the current curriculum at our university. Further work should also take into account the individual circumstances at other institutions with regard to the education plan and the use of media that promote learning.

Based on this work, we plan to evaluate an enhanced version of this VRLE with additional development stages and a combination of active and passive learning features. In a large scale investigation, we want to determine learning success by also using conventional learning methods. The goal is to establish this application as a learning aid in the curriculum of embryology. An infrastructure for this is available at our university: One possibility is a medical training center for students, where self-study learning units can take place. Thus, it should be possible for students to use this VR application in self-study, e.g. after the thematization of heart development.

9 Conclusion

In this work, we present a virtual learning environment related to embryonic heart development. Based on a user-centered design approach, the goal was to provide a platform for medical students to understand in a novel way the dynamic morphological changes that the early heart undergoes within a few days. This was reached by creating an immersive environment with interactive deformable 4D organ models. In doing so, we implemented various features to address individual learning styles to provide insight into the challenges of such applications. Based on user feedback from our evaluation with students and professionals, we envision next steps to improve this VRLE. Our work paves the way for expansion to other application areas in embryonic development and offers a promising outlook that the use of VR can improve medical education.

Acknowledgments

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