I.V. Chelpanova
Ye.V. Paltov
O.V. Smolkova
A.M. Yashchenko

Danylo Halytsky Lviv National Medical University
Lviv, Ukraine

Надійшла: 28.09.2025
Прийнята: 28.10.2025

DOI: https://doi.org/10.26641/1997-9665.2025.4.6-12

UDC: 611.12:611.013:611.061.1

METHODOLOGICAL APPROACHES TO THE STUDY OF CARDIAC SPATIAL TRANSFORMATIONS DURING ONTOGENETIC DEVELOPMENT

Chelpanova I.V. ✉, Paltov Ye.V., Smolkova O.V., Yashchenko A.M. Methodological approaches to the study of cardiac spatial transformations during ontogenetic development.
Danylo Halytsky Lviv National Medical University, Lviv, Ukraine.
ABSTRACT. Embryonic heart morphogenesis is a complex and dynamic process, and its mechanisms remain incompletely understood. A wide range of methods are used to study spatial transformations of the heart and its chambers, including histological methods, scanning electron microscopy, optical scanning microscopy, microcomputed tomography, and combinations thereof. Each method has its own advantages and disadvantages. Numerous computer models of the heart have been created, based on the analysis of well-known embryonic collections. These models have provided a thorough morphometric study of embryonic organ transformations from Carnegie stages 11 to 23 (until the end of the 8th week of gestation). However, only a few similar studies exist in the early fetal period—from the 9th to the 15th week. It should be noted that this period of intrauterine development is extremely important for the final formation of the morphological profile of many cardiac defects. Furthermore, the early fetal heart is characterized by the greatest lack of information regarding the quantitative parameters of the numerous developing structures in various cardiac chambers. Thus, many details of cardiac morphogenesis are only now being elucidated, in part due to the complex geometric transformations of the chamber cavities and wall structures. These details contribute to a better understanding of the architecture of the embryonic heart and allow for the quantitative assessment of a wide range of chamber geometric parameters and heart wall structures. They also offer a new tool for studying normal cardiogenesis and the development of congenital heart defects. This makes it crucial to use modern tools for 3D modeling of the developing heart based on visual information obtained using classical light and electron microscopy.
Key words: heart, ontogenesis, morphogenesis, spatial rearrangements, three-dimensional modeling.

Chelpanova IV, Paltov YeV, Smolkova OV, Yashchenko AM. Methodological approaches to the study of cardiac spatial transformations during ontogenetic development. Morphologia. 2025;19(4):6-12.
DOI: https://doi.org/10.26641/1997-9665.2025.4.6-12

Chelpanova I.V. 0000-0001-5215-814X; Paltov Ye.V. 0000-0002-2622-4753;
Smolkova O.V. 0000-0001-9474-7831; Yashchenko A.M. 0000-0002-8422-5834
✉ ilona.med75@gmail.com

Embryonic heart morphogenesis is a complex and dynamic process, and its mechanisms remain incompletely understood. The heart begins as a linear tube of myocardium lined with endocardial cells, undergoes looping, and develops into a four-chambered heart divided by valves and septa. This process encompasses a number of key events, including the transformation of the tubular heart into a loop, ventricular septation, and the development of the atrioventricular valvular apparatus, disruption of which leads to a large number of congenital heart defects [1-3].

A wide range of methods are used to study the shape of the heart and the relief of its chambers: his-

tological, scanning electron microscopy, optical scanning microscopy, and combinations thereof. Each has its own advantages and disadvantages [4]. Photographic images, even with a known scale, do not allow for the measurement of image depth, thereby limiting their use for determining three-dimensional spatial characteristics. A fundamentally new perspective on cardiogenesis emerges through the combination of three-dimensional reconstruction of histological sections and methods for identifying proteins and other compounds [5, 6]. This also allows for a precise understanding of the localization of various processes in the developing heart. Although the careful processing of histological sections and the use of a significant number of sections for reconstruction are time-consuming, such work allows for the highly accurate transformation of the obtained information into a spatial computer model [7, 8].

Many aspects of heart development are topographically complex and require three-dimensional reconstruction to understand the pertinent morphology. A comprehensive guide to human cardiac development, based on segmentation of structures of interest in histological sections, has been published based on a fundamental series of studies [3]. The hearts of 12 human embryos were imaged between their first appearance at 3.5 weeks and the end of the embryonic period at 8 weeks. The models were presented as calibrated interactive 3D files in portable document format (PDF). This was used to describe the appearance and subsequent remodeling of the single heart tube that occurs at the end of the fourth week after conception. Loop formation at 5 weeks, the formation of cardiac compartments at 6 weeks, and finally the septation of these compartments into physically separated left and right sides of the circulation at 7 and 8 weeks were described [3, 9].

The phases are successive, albeit partially overlapping. Thus, the basic cardiac layout is established between 26 and 32 days after fertilization and is described as Carnegie stages (CSs) 9 through 14, with development in the outlet component trailing that in the inlet parts. Septation at the venous pole is completed at CS17, equivalent to almost 6 weeks of development. During Carnegie stages 17 and 18, in the seventh week, the outflow tract and arterial pole undergo major remodeling, including incorporation of the proximal portion of the outflow tract into the ventricles and transfer of the spiraling course of the subaortic and subpulmonary channels to the intrapericardial arterial trunks. Remodeling of the interventricular foramen, with its eventual closure, is complete at CS20, which occurs at the end of the seventh week. The authors provided quantitative correlations between the age of human and mouse embryos and Carnegie developmental stages [3, 9].

Optical scanning techniques have been used to demonstrate the spatial organization of cavities in the early embryonic heart and their changes [10, 11]. Due to the limited effective depth of such research, it is only possible to study early stages and/or optically transparent specimens. The heart, smooth on the outside with a significant radius of curvature, has an exceptionally complex geometry on the inside due to the presence of trabeculae, septa, and valves. The internal surface is also the site of application of hemodynamic influences. To date, understanding of the changing geometry of the internal surface of the heart has been obtained from a small number of studies. Three-dimensional imaging methods have been used to identify features of normal and abnormal morphogenesis [12], but none of these studies have focused on quantifying the three-dimensional organization of various segments, chambers, and the heart as a whole, followed by their comparison. Determining quantitative changes in cardiac chamber volumes and geometric relationships of cavities would provide insight into the changing function of the early heart, although performing these measurements in microscopic tissues may require different imaging techniques.

One technology used to measure complex geometric shapes at low resolution is micro-computed tomography (micro-CT). Micro-CT uses high-power X-rays to image the object, converting its density gradient into a three-dimensional image. The scanning head rotates 360° around the object, creating a virtually continuous series of flat (two-dimensional) slices. Micro-CT can easily produce three-dimensional image elements smaller than 10 μm [13]. This is significantly larger than what is possible with ultrasound (30 μm) and magnetic resonance imaging (100 μm). Micro-CT is primarily used to visualize and quantify bone architecture and development [14]. Studies using radiocontrast agents have enabled the visualization of vascular structures associated with bone fracture healing, as well as the vasa vasorum, particularly the coronary arteries [15]. A potential application of micro-CT is the assessment of cardiac chamber cavities during embryonic development. Additional information will be obtained by comparing these results with serial section reconstruction and scanning electron microscopy. Unfortunately, micro-CT does not provide complete information on the volumetric parameters and chamber relationships of the developing heart.

Video light microscopy has been used to obtain real-time images of the contracting embryonic heart. This method is effective for assessing ventricular function in the early heart. However, its capabilities are limited at later stages, when only the cardiac surface can be assessed [16]. Micro-MRI (with a resolution of approximately 12 μm), which is used for in vivo imaging, is of great importance for analyzing the structure of the early heart chambers and myocardial architecture [17]. This method not only allows us to determine the spatial characteristics of the developing heart chambers but also to quantify the key structural parameters within the myocardial muscle layers [18] and evaluate the interaction between the trabecular and compact myocardium of the embryonic heart [17-

20]. However, the significant duration of the study creates certain difficulties in analyzing cardiac dynamics, as the outlines of the structures are distorted due to artifacts caused by movement during the cardiac cycle.

High-frequency ultrasound microscopy (40-100 MHz), which provides a resolution of 50 μm and a penetration depth of 4-5 mm, was used to analyze early mouse embryonic development [21]. A prerequisite for using this technique is the presence of a conductive medium or direct contact with the object being imaged.

The use of M-mode echocardiography is quite problematic in experimental animals with high heart rates, since the relaxation time of the ultrasound transducer limits the frequency at which data is recorded. The use of three-dimensional reconstruction of atrial components [22, 23] and proliferation processes in the developing heart tube [24] provided initial insights into the information that can be extracted from studying computer models of the heart.

The development of three-dimensional ultrasound cardiography has provided impetus for the study of the geometric shape of internal cardiac structures, such as fibrous rings. The spatial structure of the bicuspid valve in healthy individuals and cardiac patients has been studied in detail using three-dimensional ultrasound cardiography. Before the advent of three-dimensional echocardiography, the shape and function of the mitral valve during the cardiac cycle were studied using other three-dimensional imaging methods. It was established that the geometry of the fibrous rings changes during systole. The size of the fibrous ring is known to increase in the second half of systole after presystolic narrowing of the ring, and then continues to increase in early diastole and reaches a maximum during late diastole. Obtaining three-dimensional images using this method has certain limitations, since for spatial reconstruction of the internal structure of the heart, it is necessary to determine the appropriate anatomical landmarks before constructing the model. This approach allows for an assessment of the three-dimensional structure of the mitral and tricuspid valves, but not their volumetric relationship to the cavities during the cardiac cycle [22, 23].

Recently developed techniques, such as laser microdissection combined with quantitative polymerase chain reaction or mass spectrometry, can be used to assess certain parameters. However, their application in embryological studies is challenging due to the small size and complex morphology of the developing heart. Powerful methods such as serial gene expression analysis and microprobes provide data on gene expression but do not provide spatial information. The use of mRNA and protein identification methods, in situ hybridization, and immunohistochemistry allows localization of specific mRNA and proteins in specific cells and tissues. Combining these methods with radioactive studies and autoradiography allows calibration followed by quantitative assessment of staining intensity [22, 25]. For moderately "amorphous" organs consisting of isotropic tissue (liver), a limited number of sections can provide complete information on gene expression and its gradient. For complex objects such as the developing heart, the spatial distribution of a specific gene expression product must be mapped throughout the entire organ. In this case, studying a few random sections is insufficient.

Three-dimensional reconstructions in the study of embryonic development were initially based on the schematic delineation of the organ of interest and subsequent depiction of the reconstructed organs by medical artists [26]. With the advent of digital cameras, spatial restoration methods have become widespread. A review of previously existing reconstruction methods showed that they did not provide precise information and, at the same time, were extremely labor-intensive for researchers who implemented their reconstruction protocols using the hardware and software available at the time. Results based on the collection of episcopic images have recently been published [27]. Episcopic methods based on fluorescence allow for high-resolution imaging immediately before sectioning.

A study of the reconstructions showed that hearts at the same stage of embryonic development in the same species are identical. Carefully performed reconstructions for a single stage are apparently sufficient to create a representative model of a given developmental stage [28, 29]. The morphology of the reconstructed models corresponds to the morphology of whole-mount preparations of stained hearts. Volumetric quantitative characteristics of hearts at similar stages differ by no more than 10%. These preliminary results indicate that biological variation does not pose a problem for population assessment. It should be noted that the parameters were calculated according to Cavalieri's principle and, thus, provide an objective estimate of myocardial volumes [28].

Volumetric data on the structures of the developing heart can be used in mathematical and functional models of cardiac development. Based on these data, it was determined that a 100-fold increase in mouse myocardial volume occurs over 6 days (between days 8.5 and 14.5 of embryogenesis) [23]. Assuming that all cells in the heart undergo division during this period, this increase in volume would correspond to 6.6 cell divisions, meaning each cell should divide at least once every 24 hours. However, according to literature data and data obtained through quantitative modeling [25], cardiomyocytes differ in cell cycle duration both within the heart at a given stage and throughout the organ at different stages of development. The increase in volume can be explained not only by mitosis; other mechanisms, including cell growth, migration, and transformation, must also be

taken into account. Thus, our understanding of the dynamics of cardiac development at all stages of embryonic development will be supplemented by important information obtained through quantitative and volumetric 3D computer reconstruction [30].

The principles of muscle mechanics previously applied to the analysis of cardiac contraction focused on the need to obtain detailed information regarding the morphology of ventricular contraction. Currently, there are numerous gaps in our knowledge regarding changes in cardiac wall configuration, muscle fiber orientation, and sarcomere size during the cardiac cycle. This is necessary for constructing geometric models that analyze the mechanics of ventricular contraction, as well as for developing an understanding of the correlation between cardiac structure and function in health and disease. In situ and angiographic studies of the external and internal parameters of the left ventricle revealed changes in the shape and volume of the left ventricle during the cardiac cycle, while examination of isolated papillary muscles and the left ventricle established the relationship between sarcomere size, muscle length, and the volume of the relaxed heart [31]. However, studies of the external and internal dimensions of other cardiac chambers, as well as dynamic analysis of the cavities of the embryonic heart, were not conducted at that time.

Until now, no study has been conducted on the relief morphology and internal structure of the contracting left ventricle under known hemodynamic conditions. Methods for rapid cardiac fixation in systole or diastole, described in a number of studies, have made it possible to analyze the geometry of the ventricular cavity and walls under specific hemodynamic conditions. Information obtained through direct measurements and dynamic techniques can be applied to the development of appropriate geometric models for analyzing the mechanical properties of ventricular contraction and relaxation. Changes in the shape, volume, and thickness of the ventricular walls require the creation of a continuously changing model which, when related to established values of pressure and blood flow, would ultimately allow the accurate calculation of the distribution of stresses and shortenings of the fibers throughout the cardiac cycle.

Currently, the emphasis in such research is on studying the architecture of the cardiac chamber walls at various stages of embryonic development, taking into account changes in the orientation and distribution of muscle fibers during systole and diastole. To adequately analyze the geometry of these fibers during the cardiac cycle, it is necessary to perform three-dimensional reconstruction in combination with other morphological methods and compare the obtained results at all stages of postnatal and prenatal development, which has previously been quite difficult.

Since morphogenetic changes in the heart are spatial in nature, three-dimensional visualization and analysis of cardiac development using other methods are extremely important. Three-dimensional visualization is a powerful tool for embryological research and significantly contributes to understanding the dynamics of morphogenetic changes in the embryo [32, 33]. Attempts to three-dimensionally reconstruct embryonic structures have been made since the emergence of embryology as an independent field of study. Typically, spatial reconstruction of embryonic structures was performed based on serial histological sections of embryos, often using the wax slab technique [34]. However, such reconstruction and imaging methods require significant time and specialized skills. Recent advances in computing technology have made computer reconstruction of biological structures more efficient. Various three-dimensional structures have already been reconstructed using this method, and the simulated images can be processed at the researcher's discretion. In the field of studying the development of the heart and large vessels, computer modeling and computer graphics are used to visualize the developing heart and blood vessels of mice [12], chickens, and humans [35, 36].

Attempts have been made to reconstruct the heart and large vessels at stages of human embryonic development using computer programs. These attempts have demonstrated that computer reconstruction is an important tool for detailed analysis of the three-dimensional phenotype of embryos. During embryonic development, spatially and temporally coordinated morphogenetic changes occur. The cardiovascular system is one of the organ systems that undergoes accelerated restructuring during ontogenesis. In the earliest studies, spatial changes in the heart and great vessels of human embryos were studied using histological sections and wax-up reconstructions [37]; these studies made significant contributions to the study of human embryonic development. Studies using computer reconstruction of the heart and great vessels of normally developed embryos largely confirmed the results of these classical studies, although some inconsistencies were noted.

In a series of studies by Yamada S. et al. [32, 33], reconstruction of the structures of the cardiac cavity and great vessels of the developing human embryo using serial histological sections demonstrated their consistent spatial changes. Embryonic structures were analyzed using three-dimensional images. However, information on the cavity structures and their volumetric and morphological changes during cardiac development remained incomplete.

The successful development of methods for early prenatal diagnosis of heart defects and the development of cutting-edge micro-MRI and micro-computed tomography technologies now enable reliable three-dimensional visualization of the developing human heart, beginning as early as the 14th week of gestation [38]. These methods are inapplicable to early fetal and embryonic hearts measuring less than 8 mm. In recent years, spatial modeling methods based on a different principle—computer processing

of histological sections followed by three-dimensional reconstruction of the structures—have become dominant in embryonic heart reconstruction [3].

Numerous computer models of the heart have been created, based on the analysis of well-known embryonic collections from Carnegie, Walmsley, Boyd, Kyoto, and others [3, 35, 36, 39]. These models have provided a thorough morphometric study of embryonic organ transformations from Carnegie stages 11 to 23 (until the end of the 8th week of gestation). However, only a few similar studies exist in the early fetal period—from the 9th to the 13th week [33, 38, 39]. It should be noted that this period of intrauterine development is extremely important in terms of the final formation of the morphological profile of many cardiac defects. Furthermore, the early fetal heart is characterized by the greatest lack of information on the quantitative parameters of the numerous developing structures of various cardiac chambers [3, 39, 40].

Conclusion

Many details of cardiac morphogenesis are only now being elucidated, in part due to the complex geometric transformations of the chamber cavities and structures within their walls. These changes contribute to a better understanding of the architecture of the embryonic heart and allow for a quantitative assessment of a wide range of geometric parameters of the chambers and structures within the heart wall. They also offer a new tool for studying normal cardiogenesis and the development of congenital heart defects. This makes it crucial to use modern tools for spatial modeling of the developing heart based on visual information obtained using classical light and electron microscopy.

Information on conflict of interest

There are no potential or apparent conflicts of interest related to this manuscript at the time of publication, and are not anticipated.

References

1. Gasser RF, Cork RJ, Stillwell BJ, McWilliams DT. Rebirth of human embryology. Dev Dyn. 2014;243:621–8. doi: 10.1002/dvdy.24110.

2. Esteban I, Schmidt P, Desgrange A, Raiola M, Temiño S, Meilhac SM, Kobbelt L, Torres M. Pseudodynamic analysis of heart tube formation in the mouse reveals strong regional variability and early left-right asymmetry. Nat Cardiovasc Res. 2022; 1(5):504-17. doi: 10.1038/s44161-022-00065-1.

3. Hikspoors JPJM, Kruepunga N, Mommen GMC, Köhler SE, Anderson RH, Lamers WH. Human Cardiac Development. Adv Exp Med Biol. 2024;1441:3-55. doi: 10.1007/978-3-031-44087-8_1.

4. Azkue JJ. External surface anatomy of the postfolding human embryo: Computer-aided, three-dimensional reconstruction of printable digital specimens. J Anat. 2021;239(6):1438-51. doi: 10.1111/joa.13514.

5. Moorman AF, De Boer PA, Ruijter JM, Hagoort J, Franco D, Lamers WH. Radio-isotopic in situ hybridization on tissue sections. Practical aspects and quantification. Methods Mol Biol. 2000;137:97-115. doi: 10.1385/1-59259-066-7:97.

6. Boogerd CJ, Moorman AF, Barnett P. Protein interactions at the heart of cardiac chamber formation. Ann Anat. 2009;191(6):505-17. doi: 10.1016/j.aanat.2009.06.004.

7. Garagna S, Cebral E, Aréchaga J, Zuccotti M. Editorial: 3D Modelling of Mammalian Embryos and Organs. Front Cell Dev Biol. 2021;9:763008. doi: 10.3389/fcell.2021.763008.

8. Mori S, Shivkumar K. Stereoscopic three-dimensional anatomy of the heart: another legacy of Dr. Wallace A. McAlpine. Anat Sci Int. 2021;96(3):485-8. doi: 10.1007/s12565-021-00614-x.

9. Hikspoors JPJM, Kruepunga N, Mommen GMC, Köhler SE, Anderson RH, Lamers WH. A pictorial account of the human embryonic heart between 3.5 and 8 weeks of development. Commun Biol. 2022;5(1):226. doi: 10.1038/s42003-022-03153-x.

10. Yelbuz TM, Choma MA, Thrane L, Kirby ML, Izatt JA. Optical coherence tomography: a new high-resolution imaging technology to study cardiac development in chick embryos. Circulation. 2002;106(22):2771-4. doi: 10.1161/01.cir.0000042672.51054.7b.

11. Liebling M, Forouhar AS, Gharib M, Fraser SE, Dickinson ME. Four-dimensional cardiac imaging in living embryos via postacquisition synchronization of nongated slice sequences. J Biomed Opt. 2005;10(5):054001. doi: 10.1117/1.2061567.

12. Schneider JE, Bamforth SD, Farthing CR, Clarke K, Neubauer S, Bhattacharya S. Rapid identification and 3D reconstruction of complex cardiac malformations in transgenic mouse embryos using fast gradient echo sequence magnetic resonance imaging. J Mol Cell Cardiol. 2003;35(2):217-22. doi: 10.1016/s0022-2828(02)00291-2.

13. Guldberg RE, Lin AS, Coleman R, Robertson G, Duvall C. Microcomputed tomography imaging of skeletal development and growth. Birth Defects Res C Embryo Today. 2004;72(3):250-9. doi: 10.1002/bdrc.20016.

14. Chappard C, Peyrin F, Bonnassie A, Lemineur G, Brunet-Imbault B, Lespessailles E, Benhamou CL. Subchondral bone micro-architectural alterations in osteoarthritis: a synchrotron micro-computed tomography study. Osteoarthritis Cartilage. 2006;14(3):215-23. doi: 10.1016/j.joca.2005.09.008.

15. Duvall CL, Taylor WR, Weiss D, Guldberg RE. Quantitative microcomputed tomography analysis of collateral vessel development after ischemic injury. Am J Physiol Heart Circ Physiol. 2004;287(1):

H302-10. doi: 10.1152/ajpheart.00928.2003.

16. Shotton DM. Video-enhanced light microscopy and its applications in cell biology. J Cell Sci. 1988;89(2):129-50. doi: 10.1242/jcs.89.2.129.

17. Gilbert SH, Benoist D, Benson AP, White E, Tanner SF, Holden AV, Dobrzynski H, Bernus O, Radjenovic A. Visualization and quantification of whole rat heart laminar structure using high-spatial resolution contrast-enhanced MRI. Am J Physiol Heart Circ Physiol. 2012;302(1):H287-98. doi: 10.1152/ajpheart.00824.2011.

18. Gilbert SH, Sands GB, LeGrice IJ, Smaill BH, Bernus O, Trew ML. A framework for myoarchitecture analysis of high resolution cardiac MRI and comparison with diffusion tensor MRI. Annu Int Conf IEEE Eng Med Biol Soc. 2012;2012:4063-6. doi: 10.1109/EMBC.2012.6346859.

19. Gilbert SH, Benson AP, Walton RD, Bernus O. Slowed propagation across the compacta-trabeculata interface: a consequence of fiber and sheet anisotropy. Annu Int Conf IEEE Eng Med Biol Soc. 2011;2011:1688-92. doi: 10.1109/IEMBS.2011.6090485.

20. Gabbay-Benziv R, Reece EA, Wang F, Bar-Shir A, Harman C, Turan OM, Yang P, Turan S. A step-wise approach for analysis of the mouse embryonic heart using 17.6Tesla MRI. Magn Reson Imaging. 2017;35:46-53. doi: 10.1016/j.mri.2016.08.008.

21. Turnbull DH, Bloomfield TS, Baldwin HS, Foster FS, Joyner AL. Ultrasound backscatter microscope analysis of early mouse embryonic brain development. Proc Natl Acad Sci USA. 1995;92(6):2239-43. doi: 10.1073/pnas.92.6.2239.

22. Soufan AT, Ruijter JM, van den Hoff MJ, de Boer PA, Hagoort J, Moorman AF. Three-dimensional reconstruction of gene expression patterns during cardiac development. Physiol Genomics. 2003;13(3):187-95. doi: 10.1152/physiolgenomics.00182.2002.

23. Soufan AT, van den Hoff MJ, Ruijter JM, de Boer PA, Hagoort J, Webb S, Anderson RH, Moorman AF. Reconstruction of the patterns of gene expression in the developing mouse heart reveals an architectural arrangement that facilitates the understanding of atrial malformations and arrhythmias. Circ Res. 2004;95(12):1207-15. doi: 10.1161/01.RES.0000150852.04747.e1.

24. Van den Berg G, Abu-Issa R, de Boer BA, Hutson MR, de Boer PA, Soufan AT, Ruijter JM, Kirby ML, van den Hoff MJ, Moorman AF. A caudal proliferating growth center contributes to both poles of the forming heart tube. Circ Res. 2009;104(2):179-88. doi: 10.1161/CIRCRESAHA.108.185843.

25. Soufan AT, Ruijter JM, van den Hoff MJ, Moorman AFM. Quantitative 3d Reconstructions As Identification Tool In Heart Development. Image Anal. Stereol. 2002;20(3):193-8. doi: 10.5566/ias.v20.p193-198.

26. Verbeek FJ, Huijsmans DP, Baeten RJ, Schoutsen NJ, Lamers WH. Design and implementation of a database and program for 3D reconstruction from serial sections: a data-driven approach. Microsc Res Tech. 1995;30(6):496-512. doi: 10.1002/jemt.1070300607.

27. Ewald AJ, McBride H, Reddington M, Fraser SE, Kerschmann R. Surface imaging microscopy, an automated method for visualizing whole embryo samples in three dimensions at high resolution. Dev Dyn. 2002;225(3):369-75. doi: 10.1002/dvdy.10169.

28. Howard CV, Reed MG. Unbiased Stereology: Three-Dimensional measurement in microscopy. UK: BIOS Scientific Publishers; 1998:39–44.

29. Warmbrunn MV, de Bakker BS, Hagoort J, Alefs-de Bakker PB, Oostra RJ. Hitherto unknown detailed muscle anatomy in an 8-week-old embryo. J Anat. 2018;233(2):243-54. doi: 10.1111/joa.12819.

30. Geyer SH, Reissig LF, Hüsemann M, Höfle C, Wilson R, Prin F, Szumska D, Galli A, Adams DJ, White J, Mohun TJ, Weninger WJ. Morphology, topology and dimensions of the heart and arteries of genetically normal and mutant mouse embryos at stages S21-S23. J Anat. 2017;231(4):600-14. doi: 10.1111/joa.12663.

31. Kammern HW. [Makroskopische und mikrometrische Untersuchungen am Myokard verschfeden starkgefullter linker]. Virchows Arch. Path. Anat. Physiol. Klin.. Med. 1960;333:523. German.

32. Yamada S, Uwabe C, Nakatsu-Komatsu T, Minekura Y, Iwakura M, Motoki T, Nishimiya K, Iiyama M, Kakusho K, Minoh M, Mizuta S, Matsuda T, Matsuda Y, Haishi T, Kose K, Fujii S, Shiota K. Graphic and movie illustrations of human prenatal development and their application to embryological education based on the human embryo specimens in the Kyoto collection. Dev Dyn. 2006;235(2):468-77. doi: 10.1002/dvdy.20647.

33. Yamada S, Itoh H, Uwabe C, Fujihara S, Nishibori C, Wada M, Fujii S, Shiota K. Computerized three-dimensional analysis of the heart and great vessels in normal and holoprosencephalic human embryos. Anat Rec (Hoboken). 2007;290(3):259-67. doi: 10.1002/ar.20427.

34. Born G. [Die Plattenmodelliermethode]. Arch. Mikr. Anat. 1883;22:584–99. German.

35. Abdulla R, Blew GA, Holterman MJ. Cardiovascular embryology. Pediatr Cardiol. 2004;25(3):191-200. doi: 10.1007/s00246-003-0585-1.

36. DeGroff CG, Thornburg BL, Pentecost JO, Thornburg KL, Gharib M, Sahn DJ, Baptista A. Flow in the early embryonic human heart: a numerical study. Pediatr Cardiol. 2003;24(4):375-80. doi: 10.1007/s00246-002-0343-9.

37. Congdon E. D. Transformation of the aortic-arch system during the development of the human embryo. Contrib. Embryol. 1922;14:47–110.

38. Schleich JM, Dillenseger JL, Loeuillet L, Moulinoux JP, Almange C. Three-dimensional reconstruction and morphologic measurements of hu-

man embryonic hearts: a new diagnostic and quantitative method applicable to fetuses younger than 13 weeks of gestation. Pediatr Dev Pathol. 2005;8(4):463-73. doi: 10.1007/s10024-005-0017-8.

39. Takakuwa T. 3D Analysis of Human Embryos and Fetuses Using Digitized Datasets From the Kyoto Collection. Anat Rec (Hoboken). 2018;301(6):960-9. doi: 10.1002/ar.23784.

40. de Bakker BS, de Jong KH, Hagoort J, de Bree K, Besselink CT, de Kanter FE, Veldhuis T, Bais B, Schildmeijer R, Ruijter JM, Oostra RJ, Christoffels VM, Moorman AF. An interactive three-dimensional digital atlas and quantitative database of human development. Science. 2016;354(6315): aag0053. doi: 10.1126/science.aag0053.

Челпанова І.В., Пальтов Є.В., Смолькова О.В., Ященко А.М. Методичні підходи до вивчення просторових перетворень серця в ході онтогенетичного розвитку.

РЕФЕРАТ. Морфогенез ембріонального серця є складним і динамічним процесом, механізми якого залишаються не повністю з'ясованими. При дослідженні просторових перетворень серця та його камер використовують широкий спектр методів: гістологічні, растрову електронну мікроскопію, оптичну растрову мікроскопію, мікрокомп'ютерну томографію та їх комбінації. Кожен з методів має свої переваги та недоліки. До теперішнього часу створені численні комп'ютерні моделі серця, засновані на аналізі широко відомих ембріональних колекцій. У цих моделях проведено ретельне морфометричне вивчення ембріональних перетворень органу від 11-ї до 23-ї стадії розвитку за Карнегі (до кінця 8-го тижня гестації), проте існують лише поодинокі схожі дослідження в ранньому плодовому періоді розвитку – від 9-го до 15-го тижня. Слід зазначити, що саме даний період внутрішньоутробного розвитку є надзвичайно важливим з точки зору остаточного формування морфологічного профілю багатьох серцевих вад. Крім того, для раннього плодового серця характерний найбільший дефіцит відомостей про кількісні параметри численних структур різних відділів серця, що розвиваються. Таким чином, багато деталей морфогенезу серця з'ясовуються тільки зараз, зокрема, через складні геометричні перетворення порожнин камер і структур у складі їх стінок. Вони сприяють кращому розумінню архітектури ембріонального серця та дозволяють дати кількісну оцінку широкому спектру геометричних параметрів камер та структур стінки серця. Вони також є новим інструментом для дослідження нормального кардіогенезу та розвитку вроджених патологій серця. Це робить актуальним застосування сучасних інструментів тривимірного моделювання серця на основі тієї візуальної інформації, що отримана за допомогою класичних методів світлової та електронної мікроскопії.

Ключові слова: серце, онтогенез, морфогенез, просторові перебудови, тривимірне моделювання.