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Three-dimensional echocardiography: technical aspects and imaging modalities☆

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Abstract Real-time three-dimensional echocardiography (RT3DE) is increasingly available in the veterinary field due to continuous reduction in costs and improvement of equipment. Much like its motion-mode and bi-dimensional counterparts, acquisition and analysis of RT3DE images and datasets is greatly improved by a thorough understanding of the technological aspects, basic physic principles, and knowledge of available modalities with their advantages and drawbacks. In this review, the authors aim to describe how the currently available RT3DE technology has evolved, explain technical aspects of the equipment, and illustrate the most commonly available modalities for image acquisition and visualization.

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Historical aspects

'A system for ultrasonically imaging the human heart in three dimensions' was first described by Dekker et al. in 1974 [1] The system consisted of an ultrasonographic transducer connected to a mechanical arm with five degrees of freedom to detect transducer position and aim (Fig. 1). The acquired two-dimensional (2D) images were stored based on transducer location, and the system would then allow the offline manipulation of the dataset acquired. Efforts were then invested in miniaturization of the transducer's tracking system with the development of 'free-hand' (i.e. not attached to a mechanical arm) acoustic (spark gap) [2], electromagnetic or optical sensors. Most of these systems could be outfitted on regular transducers, but clinical implementation was hindered by limitations related to the size of the locators as well as the time-consuming process of image creation and analysis. In an attempt to resolve some of these limitations, other approaches sought the acquisition of consecutive 2D planes by either linear, fan-like, or rotational standardized motion of the transducer. The set of images (datasets) acquired, were automatically stitched together and interpolated by computer software [3—5]. As it is often the case, early experiments for equipment validation included echocardiographic evaluation of several mammalian hearts such as cows, dogs, goats, and pigs [6—10].

The next and possibly most important technological breakthrough however came from implementation of the capability of acquiring volumes, rather than sequential sets of single 2D planes. This was achieved by researchers at Duke University by arranging phased-array piezoelectric elements in multiple rows rather than just one marking the beginning of real-time three-dimensional echocardiography (RT3DE) [11—13]. Recent evolutions essentially refine and further develop the same type of technology taking advantage of the overall exponential progresses in the fields of data optimization, increase in bandwidths of data transfer and processing, and system miniaturization that allow to have continuously smaller transducers, faster volume rates, higher definition.

Technical principles

As it can be appreciated from the previous section, the key component of RT3DE is the transducer. Currently, commercially available RT3DE transducers are often called matrix array probes because the piezoelectric elements are arranged in a grid of rows and columns (matrix) for a total of thousands of single elements. In a 2D ultrasound transducer, each piezoelectric element is connected by its own cable to the echocardiographic machine, where a technique called *beamforming* processes the signals both in the phases of transmission and reception in order to obtain focused beams. If the same approach was taken for RT3DE transducers, this would result in an unpractical amount of wiring as well as a very large circuit board requiring massive amount of power. To overcome this limitation, matrix transducers employ several smaller circuit boards that group small arrays of elements (patches) directly in the probe, a process known as *microbeamforming* [14]; this allows modern RT3DE transducers to have dimensions and cables that are comparable to 2D ones.

The speed of ultrasound in tissue (i.e. approximately 1540 m/s) provides a further impediment in RT3DE; when applied to a pyramidal beam, regular ultrasound transducer's scanning techniques would result in such a low volume rate — measured in volume per second, the RT3DE equivalent of frame rate — that it would be clinically useless. Once again thanks to engineering ingenuity a process called *parallel receiving beam* was implemented for RT3DE transducers in which for each beam transmitted, the probe

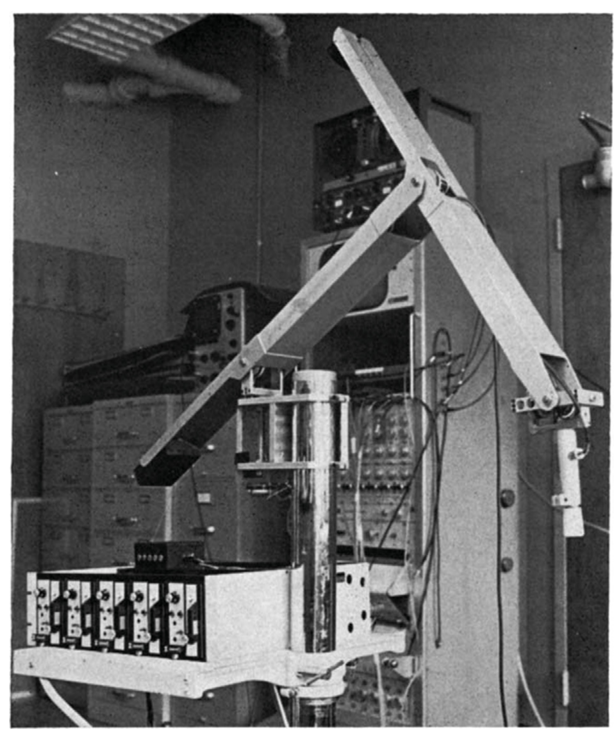

Figure 1 Photograph of the five degrees of freedom arm including signal conditioners and stand. Reprinted with authorization from Dekker et al. Computers and Biomedical Research 1974.

receives and analyzes multiple parallel beams, therefore greatly increasing the volume rate of acquisition [15,16]. However, this comes at the expense of the signal-to-noise ratio and resolution. Therefore, other techniques and image acquisition modalities (i.e. 3D Zoom, multi-beat acquisition) have been developed in an attempt to provide both higher temporal and spatial resolution. Another important consideration for optimizing RT3DE acquisitions comes from understanding the system's *point spread function*. Simply put, the point spread function of an optical system is the degree of blurring in the representation of an otherwise point object [17]. The point spread function of RT3DE systems is minimal in the axial dimension, while maximal in the elevation [15]. Therefore, less blurred images of a certain cardiac structure will be obtained by using the axial dimension (X-axis) for its representation (Fig. 2). For properly using and implementing RT3DE in the clinical settings, it is important to understand the strengths and weaknesses of each acquisition modality as they are often used in combination during a specific echocardiographic study depending on the specific need or structure to be visualized.

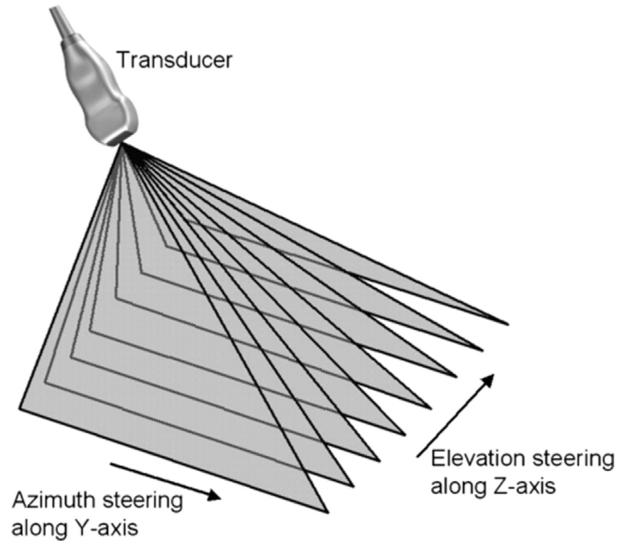

Figure 2 Three-dimensional echocardiography transducers. The three-dimensional (matrix) transducer's beam is pyramidal, therefore, there is also an 'elevation' component. Reprinted with authorization from Wang XF, Deng YB, Nanda NC, Deng J, Miller AP, Xie MX. Live three-dimensional echocardiography: imaging principles and clinical application. Echocardiography. 2003 Oct; 20(7): 593—604. https://doi.org/10.1046/j.1540-8175.2003.03106.x. PMID: 14536007.

Image acquisition modalities

Multi-plane acquisition

It is important to differentiate multi-plane acquisition from multi-plane visualization. The latter is most often used as part of full-volume or multi-beat acquisition modalities and will be covered in the next section. Multi-plane acquisition instead is a real-time technique in which only selected lines of piezoelectric elements are fired simultaneously. This results in visualization of two or more simultaneous 2D images with high resolution and frame rate (Fig. 3). The visualized planes are the only ones acquired, unless another modality is simultaneously activated. This technique has proven particularly useful in recent years for guidance of advanced interventional or hybrid cardiac procedures where maneuvering and deployment of intracardiac devices require both accurate spatial resolution and high frame rates [18].

Full-volume acquisition

The most intuitive and straightforward RT3DE acquisition modality, in full-volume acquisition of a pyramidal volume, is acquired and visualized in real-time. Its main advantage, besides the ease of use, is that since the entire pyramidal volume is acquired, cropping and analyses can be performed both during the acquisition and in post-processing. However, as previously described, this technique often provides somewhat lower resolutions and/or slow volume rates, particularly compared to the average cycle length of unsedated small animals during echocardiographic examinations.

Multi-beat acquisition

Multi-beat acquisition is a modality in which the machine divides the full volume to be acquired in smaller sub-volumes. Each sub-volume is then acquired during consecutive heartbeats (commonly four or six) and stitched together to provide a wide volume of acquisition with high spatial and temporal resolution (high volume rate). Electrocardiographic gating is necessary, and it ensures that the sub-volumes are acquired during the same phase of the cardiac cycle. Respiratory gating, or breath-hold during acquisition, is also used in humans, but impossible or impractical to implement in veterinary medicine. The biggest pitfall of this modality is that it relies on the consistent position of the structures insonated during several cardiac cycles. For this reason, sinus arrhythmia (which continuously changes the cycle length on a beat-to-beat basis), respiratory motion, and slight transducer movement

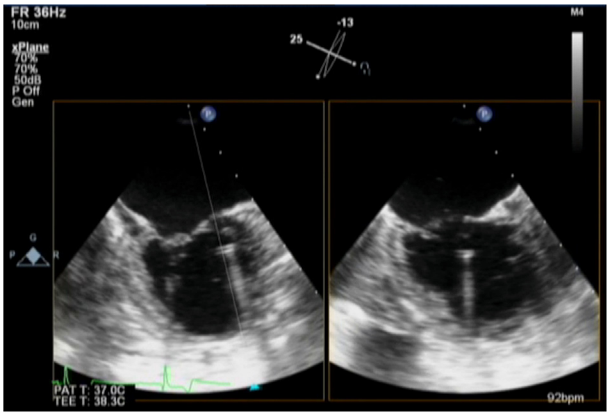

Figure 3 Multi-plane image acquisition. During this multi-plane acquisition two orthogonal planes are simultaneously visualized. The one on the left is used as a reference and a line (white arrows) can be swung to select the location of the orthogonal plane showed on the right. In this case, the line is used to follow and guide the movement a device introduced through transapical approach and visible in the left ventricle in both planes (green arrow).

during the acquisition can result in *stitching artifacts*, where the different sub-volumes are not properly aligned to each other with resultant artifactual tissue discontinuation (Fig. 4 and Video 3). Nonetheless, when stitching artifacts can be prevented, this modality results in acquisition of a very large RT3DE dataset, usually containing the entire heart, with high volume rates, a very important factor for small animals. Datasets can then be analyzed offline for visualization and quantification of several different cardiac structures [19—25].

Three-dimensional zoom

In *3D Zoom* modality, the operator selects the position and size of a 'sample box', smaller than the full volume, to encompass only the structure(s) or region of interest. The box size and position are usually adjusted from simultaneous live multi-plane 2D images. Once the *3D Zoom* function is triggered, only the smaller volume of the box is visualized *en face* (looking to it usually according to blood flow, for example atrial side for atrioventricular valves and ventricular side for semilunar valves) and acquired. The biggest advantage of this technique is the rapid evaluation of a specific region of interest, without the need for labor-intensive cropping and orientation. Furthermore, since a smaller volume is acquired, this results in higher volume rates and resolution compared to a full-volume acquisition. The most common application of this modality is probably transesophageal evaluation of cardiac valves, congenital defects, and guidance of intracardiac devices (Fig. 5, Video 4). A drawback of this modality is that the operator can lose the relationship between the visualized structures and the surrounding ones.

Three-dimensional color Doppler

As per its 2D counterpart, a color Doppler region of interest can be over-imposed to multi-plane or three-dimensional images (either *Full Volume, Multi-beat, or 3D Zoom*). When applied to three-dimensional imaging, the region of interest is pyramidal as well, providing theoretically a more accurate evaluation of flows' geometries and direction. This would overcome many limitations of conventional color Doppler techniques like, for example, quantification of flow through non-circular orifices, eccentric jets, and wall-hugging flows [26—28]. This technique has indeed already been used in veterinary medicine for evaluation of effective regurgitant orifice area [25]. One of the main limitations that currently prevents the clinical widespread of this technique is the low volume rate achievable with current technology.

Image visualization and post-processing

Visualization of 3D images is a challenge on its own. Stereoscopic vision allows the operator to actually see images in three dimensions and although it is likely to be increasingly adopted in the future, the requirement for special monitors and eyewear are limitations to its widespread adoption [29]. Besides *multi-plane acquisition* and *multi-plane visualization*, the other RT3DE modalities face the challenge of representing 3D images on a 2D screen. Several solutions have been implemented and different visualization modalities are available for RT3DE; these can be used in isolation or in combination for obtaining different information from the data acquired.

Multi-plane visualization

Multi-plane visualization, also called multiplanar reconstruction by some vendors, is usually available both during acquisition (live), and during post-processing of RT3DE and color RT3DE images. In contrast to *multi-plane* acquisition, in this modality, the volume acquired is three-dimensional and for this reason, virtually any 2D cut plane can be selected to 'slice' the 3D volume. Furthermore, several different 2D image planes can be simultaneously visualized. Most commonly, a primary cut plane is selected in the

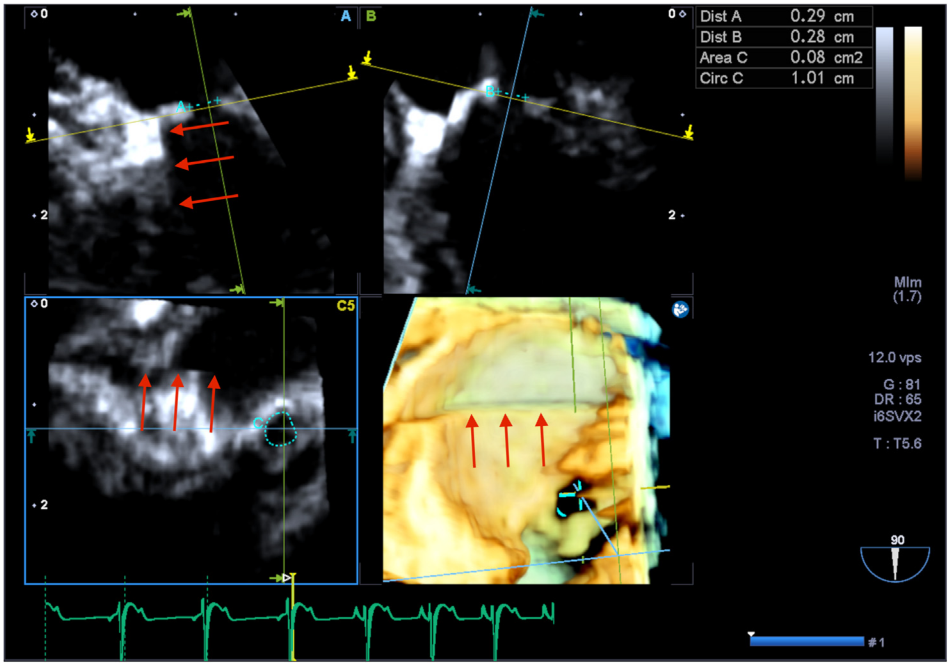

Figure 4 Stitching artifacts. Real-time three-dimensional transesophageal echocardiography of a stenotic pulmonic valve. The images were acquired with multi-beat acquisition and a stitching artifact is clearly visible as a straight line of misalignment in all the two-dimensional and three-dimensional planes (red arrows). Multi-plane visualization was also used for measuring both the diameters and the area of the stenotic orifice.

reference image and several other orthogonal and parallel planes are visualized (multiplanar visualization) (Figs. 4—6). This modality allows precise alignment with cardiovascular structures of interest and complex multi-level functional assessments, like assessment of minimal stenotic orifices or stress echocardiography [30,31]. In veterinary medicine, this technique was used for assessing mitral regurgitant effective and anatomic regurgitant areas [19,25,32,33].

Volume rendering

Volume rendering is probably the most common RT3DE visualization modality. In these images, the surface of cardiac structures is rendered by converting voxels (the smallest discrete element of a three-dimensional image) into pixels. Two main controls — a threshold value and a transparency value — can be manually adjusted to determine what appears solid vs. transparent. The perception of depth is created by ingenious use of different color intensities and hues of each pixel [34] with lighter colors used for near structures (most commonly represented in shades of yellows) while darker colors (usually shades of blue) are used for farther structures.

Volume-rendered images can be manipulated either live or offline by processes of orientation, slicing, and cropping. Orientation is the most intuitive one and consists of moving the image around a fixed point to obtain the best viewpoint for the structure of interest. Slicing most commonly indicates the use of several parallel sliced planes from the RT3DE volume, while cropping is the process through which any image plane is used to 'cut' through the acquired volume and obtain visualization of the structures cut by this plane. It is worth noticing that this increased capability of freely orienting and cutting through cardiac structures poses the problem of nomenclature standardization. This issue has been addressed in the human field by Nanda et al. [35] and then adopted by the European Association of Echocardiography and American Society of Echocardiography [34]. Since the described nomenclature uses planes relative to the heart itself rather than the heart orientation to the body, this can be easily applied to animals as well and the authors of this paper support the adoption of this nomenclature in veterinary RT3DE applications. Briefly, transverse planes are perpendicular to the long axis of the heart and each divide it into two segments, one viewed 'from apex', the other 'from base'; the sagittal plane is a longitudinal plane that divides the heart into two segments, one viewed 'from the left', the other 'from the right'; and the coronal plane, divides the heart

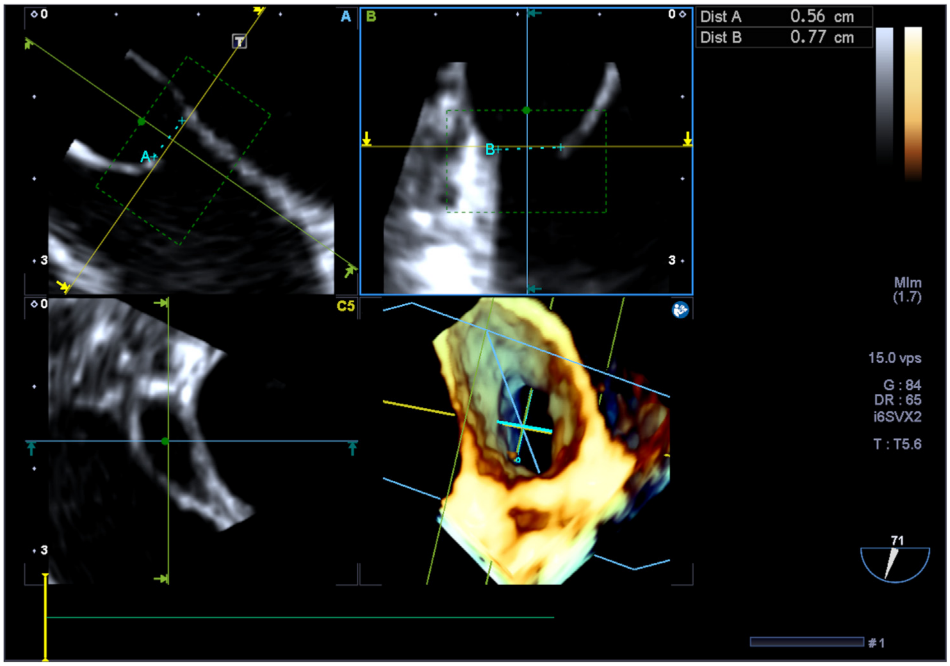

Figure 5 Transesophageal three-dimensional *en face* view of a patent ductus arteriosus. A small box (green dashed rectangles) is selected and oriented so that the structure of interest is visualized in three-dimensions from a preferential point of view (green dot on the dashed boxes). In this example, transesophageal echocardiography was used to visualize a patent ductus arteriosus minimal ductal diameter *en face* from the ampulla, looking towards the pulmonary artery. Furthermore, multi-plane visualization was used to assess the ductus. Each plane is color coded for ease of interpretation: the yellow line in panels A and B, is the C5 plane; the green line in panels A and C5 is plane B; the blue line in panels B and C5 is plane A. The planes were aligned to measure the ductus from several orthogonal views that were aligned with the ductus' main axes. As can be noted from the three-dimensional image as well as plane C5, the ductus is very oval with the wider diameter (Dist B) ~40 % bigger than the shorter one (Dist A).

vertically into two segments, one viewed 'from above', the other 'from below' (Fig. 7).

Recently, two more options for volume rendering visualization were developed: trans-illumination and transparency rendering. These are also called photorealistic renderings. In these modalities, tissue is usually colored in shades of pink, more closely resembling the real color of cardiovascular structure, and the operator can both define the level of transparency of tissue and shine a virtual light source that is freely movable to highlight the structures of interest (Videos 1 and 2 — Supplemental material). These techniques are receiving great attention in recent years in the human medical field as they seem to improve the diagnostic utility of RT3DE [36—39].

Surface rendering

In this modality, the structure of interest is traced either manually or through a semi- or fully-automated process and then represented as a cast model. The model can either be represented as a wire frame, in which the surface is divided into a

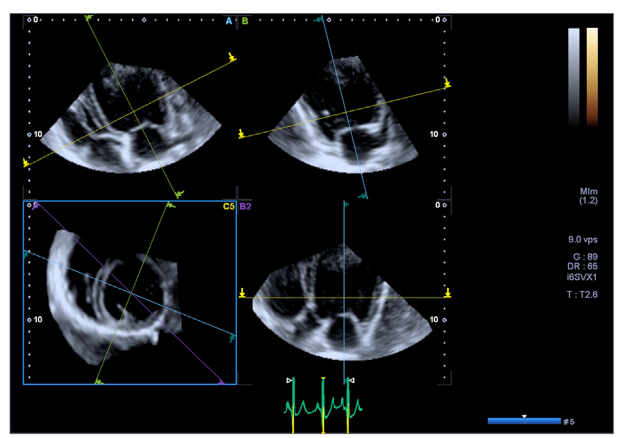

Figure 6 Multi-plane visualization. After a full-volume acquisition, virtually any cut plan can be obtained and visualized simultaneously. In this example, four planes were aligned to show a standardized apical four-chamber view (top left), a two-chamber view (top right), a short axis at the level of the papillary muscles (bottom left), and a left ventricular inflow-outflow view (bottom right). Note that, for ease of interpretation, the planes are color coded. For example: panel B — green, top right — shows the plane that is cut by moving the green line visualized in panels A and C5.

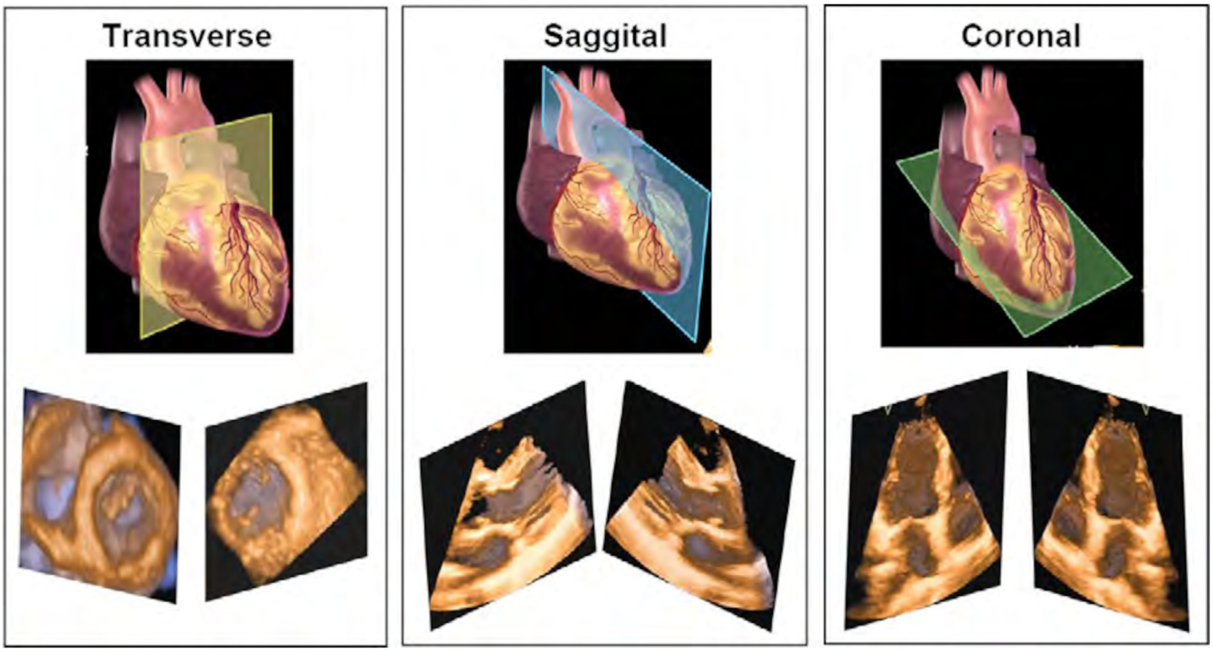

Figure 7 Standardized cropping planes. Transverse planes are perpendicular to the long axis of the heart and each divide it into two segments, one viewed 'from apex', the other 'from base'; the sagittal plane is a longitudinal plane that divides the heart into two segments, one viewed 'from the left', the other 'from the right'; and the coronal plane, divides the heart vertically into two segments, one viewed 'from above', the other 'from below'. Reprinted with authorization from Lang et al. J Am Soc Echocardiogr 2012.

pre-determined number of small geometrical sub-segments, or as a solid object (Fig. 8). Furthermore, the information derived from complex analyses can be color-coded and visually represented on the cast's surface for more readily available interpretation, like for example areas of high or low strain on a ventricle, or prolapsing portions of atrioventricular valves (Fig. 9).

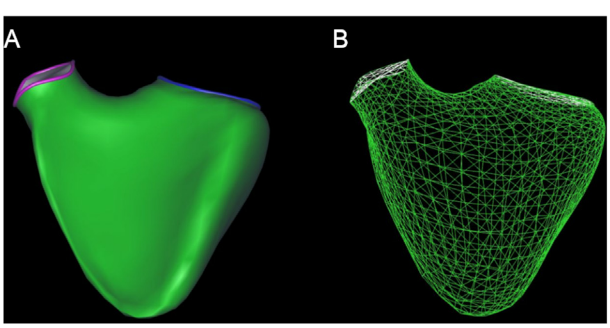

Figure 8 Surface rendering of the right ventricle. These surface renderings of the right ventricle were obtained by a semi-automated analysis of transthoracic full-volume multi-beat real-time three-dimensional echocardiographic acquisition of a dog. After tracing the contours of the right ventricle, the software[e] creates a model of the ventricle that can be represented as a solid object (A) or mesh (B). The complex shape of the right ventricle can be clearly appreciated. These images were oriented so that the pulmonic valve is on the left, purple ring on the solid rendering, while the tricuspid annulus is on the right (blue ring).

Post-processing

As it can be inferred from some of the previous sections, one of the biggest advantages of RT3DE is the extremely wide range of image analysis and visualization possible from a single acquisition. Most human and veterinary echocardiographic

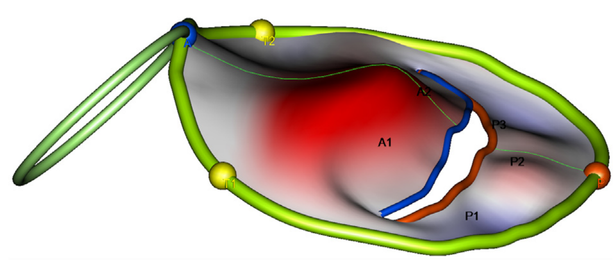

Figure 9 Mitral valve model showing prolapse. A model of the mitral valve was created by semi-automated analysis of transthoracic full-volume multi-beat real-time three-dimensional echocardiographic acquisition of a dog using dedicated software[f]. A mid-systolic frame is shown. Areas of prolapse are colorized by the software in red. It is immediately evident a prolapse of part of A1 scallop and the entire A2 scallop of the mitral valve. There is also lack of leaflet coaptation and the valve annulus appears somewhat flat.

Figure 10 3D printed models of canine mitral valves. The mitral valves of two canine patients were 3D printed based on real-time three-dimensional echocardiographic images. The valves were magnified (2×) to emphasize differences in order to be used for teaching purposes. It can be appreciated how the valve on the left has a flat annulus and an anterior leaflet prolapse as consequence of myxomatous valvular degeneration, while the one on the right is from a healthy dog and has a clear saddle-shape. The thin nature of valves presents a challenge for 3D printing. For example, these models were created by stereolithography, since the more common fused deposition modeling printers were not able to represent fine details appropriately. The support structure is automatically created by the 3D printing software and can be cut out from the valve model if needed.

laboratories use RT3DE as an addition to conventional echocardiography. However, with further technological development, it is not unreasonable to think that in the future a comprehensive echocardiographic evaluation could be performed by only acquiring RT3DE images. In the authors' laboratories, for example, the same full-volume multi-beat acquisition dataset can be analyzed using different software packages[d–g] in order to obtain left and right ventricular volumes, stress and strain, left and right atrial volumes, anatomic regurgitant orifice areas, and advanced morphologic analysis of the mitral valve. One of the disadvantages of these software packages is that they rely on proprietary software algorithms for calculations and, therefore, require a 'leap of faith' from the operator. Nonetheless, the vast majority of softwares leave full control to the operator to verify and correct semi-automated tracking; furthermore, since the images analyzed are three-dimensional, the ultrasonographer's effect on the data is logically less relevant, as problems related to oblique or not aligned image planes is virtually nonexistent. It is now clearly recognized in humans that, given the complex shape of cardiac structures, RT3DE provides superior assessment than conventional echocardiography for volumetric and functional assessments since it does not rely on geometrical assumptions [34]. Validation of RT3DE in veterinary medicine is limited by availability and intrinsic limitations of gold standard methods, such as cardiac magnetic resonance image, computed tomography, thermodilution — nonetheless, many studies have already been undertaken [40–49].

Lastly, it is also important to notice how RT3DE datasets allow the performance of conventional 2D measurement, as the images can be sliced, cropped, and rotated to visualize standardized 2D image planes that can be then measured as previously (Figs. 4–6).

Three-dimensional printing

Printing from RT3DE images is feasible, although definitely not as straightforward as printing regular echocardiographic images. A detailed description of the process is beyond the scope of this review; however, some key points will be presented. Briefly, several different types of 3D printers are commercially and professionally available, and the characteristics of the printing media as well as the printing modality should be taken into account when considering the final product and its intended use. The input required by most 3D printers is a virtual model in the format of an.STL file. Generation and optimization of such files before printing usually requires one, or often more than one, dedicated software package and expertise. Nonetheless, direct export to.STL files is increasingly being embedded in RT3DE software packages while the cost of 3D printing is exponentially decreasing and with it, its availability increasing in similar fashion (Fig. 10).

Final remarks

Implementation of RT3DE in veterinary echocardiography laboratories is slowly but steadily happening. Technological progresses are constantly improving this technology making it more affordable, user-friendly, and capable of acquiring images with higher definition and faster volume rates through smaller probes' footprints, hence better suitable to image most veterinary patients.

[d] 4D LV-ANALYSIS 3, TOMTEC Imaging Systems GmbH, Unterschleissheim, Germany.
[e] 4D RV-FUNCTION 3, TOMTEC Imaging Systems GmbH, Unterschleissheim, Germany.
[f] 4D MV-ASSESSMENT 2, TOMTEC Imaging Systems GmbH, Unterschleissheim, Germany.
[g] 4D CARDIO-VIEW 3, TOMTEC Imaging Systems GmbH, Unterschleissheim, Germany.

Nonetheless, as any new technique, operators face a steep learning curve in the process of image acquisition, optimization, and analysis. Most newer echocardiographic machines can now integrate 3D analysis software packages directly on the cart, while some advanced analyses still require a dedicated workstation.

Author contributions

All the authors have substantially and equally contributed to the writing and revision of this review manuscript. All the authors approve the final version to be published.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jvc.2023.11.010.

Video 1 Half-speed photorealistic rendering of a dog with bileaflet mitral valve prolapse. Three orthogonal two-dimensional image planes are simultaneously visualized (top left, top right, bottom left) and used to crop a three-dimensional *en face* visualization of the mitral valve (bottom right). The mitral valve is visualized *en face* (looking from the left atrium) and is oriented with the aorta at twelve o'clock using a clock-face analogy. Photorealistic rendering is utilized and during the video, the operator is moving the light source (the position of which is displayed on the blue sphere at the bottom right corner of the image) casting shadows that emphasize different aspects of the valve. A bileaflet prolapse can be appreciated both from two-dimensional and three-dimensional images.

Video 2 Photorealistic rendering of subaortic stenosis. This clip shows a photorealistic rendering obtained from a dog with subaortic stenosis. The image is cropped and oriented so that left ventricular inflow and outflow are visualized as seen from the left ventricle and main structures are labeled at the beginning of the clip. A prominent ridge can be visualized in the left ventricular outflow tract, below the aortic valve. Ao: Aorta; MV: Mitral valve; SAS: subaortic stenotic ridge.

Video 3 Pulmonic stenosis and stitching artifacts. Clip of the same dog in Fig. 4 affected by valvular pulmonic stenosis. Multi-plane visualization was used to align the two-dimensional planes with the stenotic orifice and measure its diameters and area. The panel in the bottom right shows a surface rendering of the pulmonic leaflets and stenotic orifice visualized from the post-stenotic dilatation. Stitching artifacts can be noted crossing the image in all the two-dimensional planes as well as in the surface rendering.

Video 4 Surface rendering of a deployed Amplatz Canine Duct Occluder. Surface rendered image obtained after successful deployment of an Amplatz Canine Duct Occluder. This image was obtained with multi-beat acquisition and then cropped in order to visualize only the device, which has normal, unstressed conformation. Notice the level of detail of the rendering that can be obtained with this technique.

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