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Original Article

Magnetic resonance of hearts in a jar: breathing new life into old pathological specimens

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Abstract *Background:* Specimens of the normal and congenitally abnormal heart have been long preserved, collected, and studied. It is increasingly difficult to add to such pathological collections. These museum pieces are often inaccessible for teaching purposes. Magnetic resonance imaging of old pathological specimens could produce high-resolution unalterable datasets that could be processed to create three-dimensional reconstructions using inexpensive systems that could be used by untrained individuals. To our knowledge, the concept of "Virtual Autopsy" has not been applied to cardiac specimens of museum collections. *Methods:* To determine optimal sequences and assure specimen safety, five different pulse sequences designed to create three-dimensional datasets were tried on a uterus specimen suspended in a fluid-filled glass container, using a 1.5 Tesla scanner with an eight-channel phased-array coil. Having found the best sequences and established specimen integrity, we scanned six historical heart specimens in their original fluid-filled glass containers. The datasets were processed on a laptop with a DICOM viewer available as freeware. *Results:* All specimens were successfully scanned. The best image quality was obtained by using a three-dimensional FSPGR and the BRAVO pulse sequences. High-resolution three-dimensional and multi-planar image processing was possible for all datasets. Detailed examination of the specimens could be easily performed. *Conclusion:* Pathological specimens can successfully be scanned in minutes resulting in unalterable and portable high-resolution three-dimensional datasets that can be processed by using inexpensive readily available software. The final cardiac reconstructions can be widely shared for educational and scientific purposes and ensure a lasting access to pathological specimens.

Keywords: Congenital cardiac disease; cardiac pathology; virtual autopsy; web-based teaching

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To better understand cardiac embryology and anatomy, specimens of the normal and congenitally abnormal heart have been long preserved, collected, and studied. It is increasingly difficult to add to such pathological collections as few patients with congenital cardiac defects die without prior surgery and legislation may limit long-term preservation of contemporary specimens. McGill University's Pathology Department is the custodian of several very old historical specimens such as the "Holmes Heart" that dates back to 1823, and many congenitally malformed hearts described and preserved by the celebrated Maude Abbott. McGill's pathology museum collection consists of pre-dissected heart specimens mounted with glass rods and silk threads, suspended in sealed glass containers filled with Kaiserling III solution. While extremely interesting and unique, these pieces are seldom moved due to their fragile state and thus are accessible only to individuals who can view them personally on the museum's shelves.

We hypothesised that these historical pathological specimens could be safely imaged in their original fluid-filled containers using a conventional magnetic-resonance scanner and commercially available pulse sequences, that one could generate comprehensive

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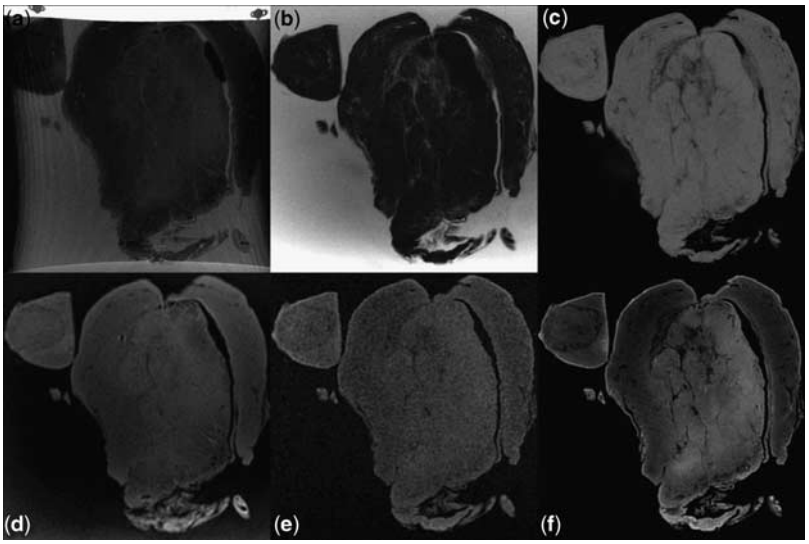

Figure 1.
*Examples of five pulse sequences used on a test specimen of a uterus and placenta: (**a**) three-dimensional FIESTA, (**b**) two-dimensional FSE T2, (**c**) two-dimensional FSE T2 with inverse grey scale, (**d**) two-dimensional FSE T1, (**e**) LAVA, and (**f**) three-dimensional FSPGR sequences. The three-dimensional FSPGR sequence had the best signal-to-noise ratio, best contrast with the liquid media, and best image definition.*

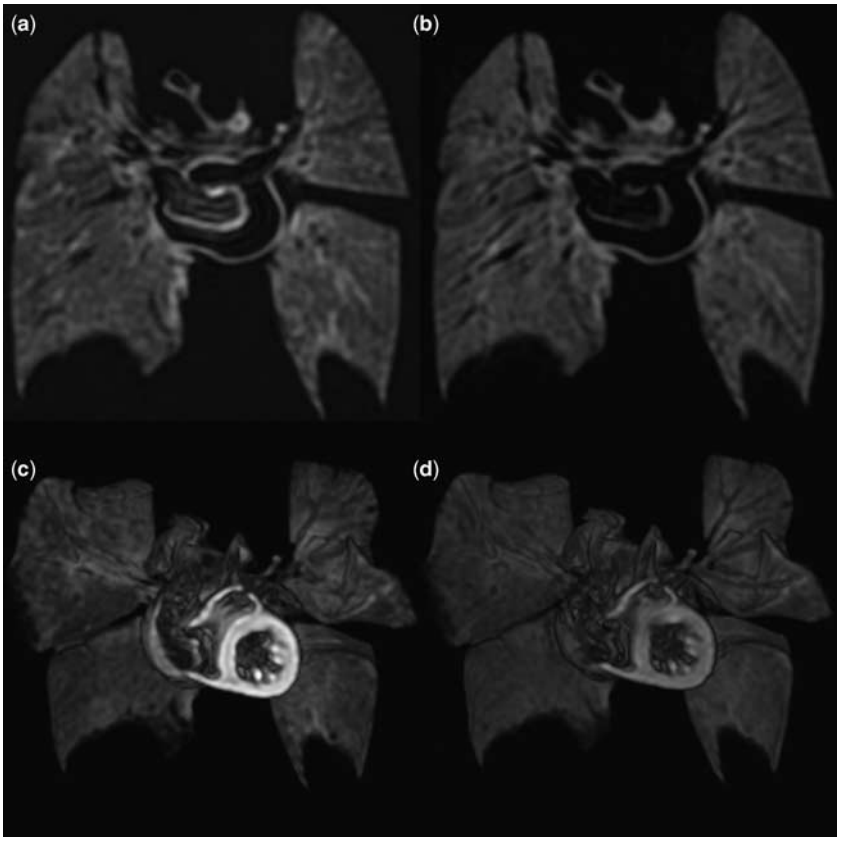

Figure 2.
*Comparison of source images and three-dimensional renderings from two pulse sequences applied to the a specimen of normal newborn heart; the three-dimensional FSPGR sequence on the left in (**2a**, **2c**), and the BRAVO sequence on the right in (**2b**, **2d**). Both sequences had equivalent signal-to-noise ratio, contrast with the liquid media, and image definition. The resulting three-dimensional renderings were nearly indistinguishable.*

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Table 1. Pulse sequences and imaging parameters used for the specimens.

Pulse sequence	Three-dimensional FSPGR*	BRAVO*	LAVA*	Three-dimensional FIESTA*	Two-dimensional FSE T1*	Two-dimensional FSE T2*
Coil	Eight-channel body, eight-channel head	Eight-channel head	Eight-channel body	Eight-channel body	Eight-channel body	Eight-channel body
Imaging options	Fast, Zip2, Zip512	Fast, Ir p, Zip2, Zip512	Exended dynamic range, Zip2, Zip512	Fast, Zip2, Zip512	Fast, Zip2, Zip512	Fast, Zip2, Zip512
Flip angle	55–60	15–20	15	55	90	90
TE (msec)	Minimum full	Pre-determined	Pre-determined	Minimum full	Minimum full	102.7
TR (msec)	5.1	Pre-determined	Pre-determined	4–6	400	3000–4000
Inversion time (msec)	Not applicable	200–300	Not applicable	Not applicable	Not applicable	Not applicable
Echo train length	1	1	1	1	3	16
Receiver bandwidth (khtz)	31,25	31,25	62,5	62,5	31,25	31,25
Field of view (cm)	25	16–25	25	25	25	25
Slice thickness (cm)	1	1	1	1	2	2
Matrix size	224 × 224	224 × 224	224 × 224	224 × 224	224 × 224	224 × 224
Number of averages	4	1	1	4	3	3
Phase field of view	1	1	1	1	1	1
Frequency direction	Superior–inferior	Superior–inferior	Superior–inferior	Superior–inferior	Superior–inferior	Superior–inferior

Ir p, inversion recovery preparation

*Three-dimensional-SPGR sequence (a three-dimensional fast spoiled gradient recalled acquisition in the steady state), BRAVO sequence (a fast inversion-recovery prepared three-dimensional gradient echo sequence), three-dimensional-LAVA sequence (a three-dimensional fast turbo gradient echo sequence with T1 weighting), three-dimensional FIESTA (a three-dimensional balanced steady state free precession acquisitions), three-dimesional FSE T1 (a two-dimensional fast spin-echo T1 sequence), and two-dimensional FSE T2 (a two-dimensional fast spin-echo T2 sequence)

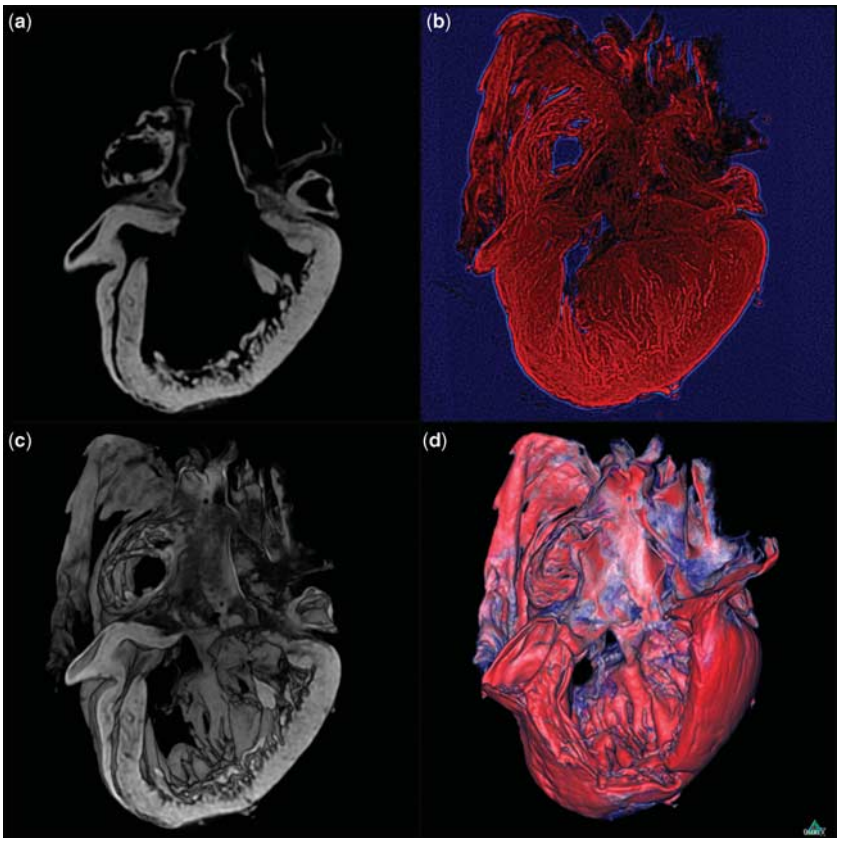

Figure 3.
*From source image to three-dimensional reconstructions: (**a**) three-dimensional FSPGR slice from the original dataset, (**b**) textured maximal intensity projection images to depict the myocardial ultra structure, (**c**) thick-slab volumetric rendering, and (**d**) three-dimensional model of the "Holmes Heart". Note how the thick-slab volumetric rendering shows the vestigial chamber beyond the bulboventricular foramen.*

high-resolution datasets, that these datasets could be used to generate sophisticated three-dimensional renderings and reconstructions. Our goal was to provide digital tools through, which the teaching and scientific value of historical specimens could be preserved, and widely shared.

Although magnetic resonance has been used to image pathological specimen, to our knowledge, the concept of "Virtual Autopsy" where comprehensive computerised tomography or magnetic-resonance imaging datasets are used to generate sophisticated and geometrically accurate three-dimensional renderings and models, has not been applied to cardiac specimens from museum collections.[1–4]

Materials and methods

To determine optimal sequences and ensure specimen safety we subjected an undated specimen of a uterus to 3 three-dimensional and 2 two-dimensional magnetic-resonance sequences. The three-dimensional sequences were designed to create a dataset with a native voxel size of 1 cubic millimetre, whereas the two-dimensional sequences had a voxel size of $1 \times 1 \times 2$ millimetre. Having found the best sequences and confirmed specimen integrity we scanned historical specimens of a vascular ring, the heart and lung of a normal newborn, the heart and lung of a newborn with pulmonary atresia with ventricular septal defect, a heart specimen with an atrioventricular septal defect, the heart of a small shark, and the famous "Holmes Heart".[5] We also tried an additional three-dimensional sequence on three of the specimens as they were small enough to fit in a high definition eight-channel head coil.

The specimens were imaged within their sealed fluid-filled glass containers; once all metal structures on the outside of the containers (such as metal brackets to hold labels) were removed. The containers were positioned on a gel pad within the magnet and securely fastened to minimise the transmission of vibrations to the specimen.

An eight-channel transmitter-receiver body coil and, on the smaller specimens, an eight-channel high definition head coil, were used in a 1.5 Tesla scanner, General Electric Medical Systems, Milwaukee, Wisconsin, United States of America, version HDX. We used a standard 3D FSPGR sequence,

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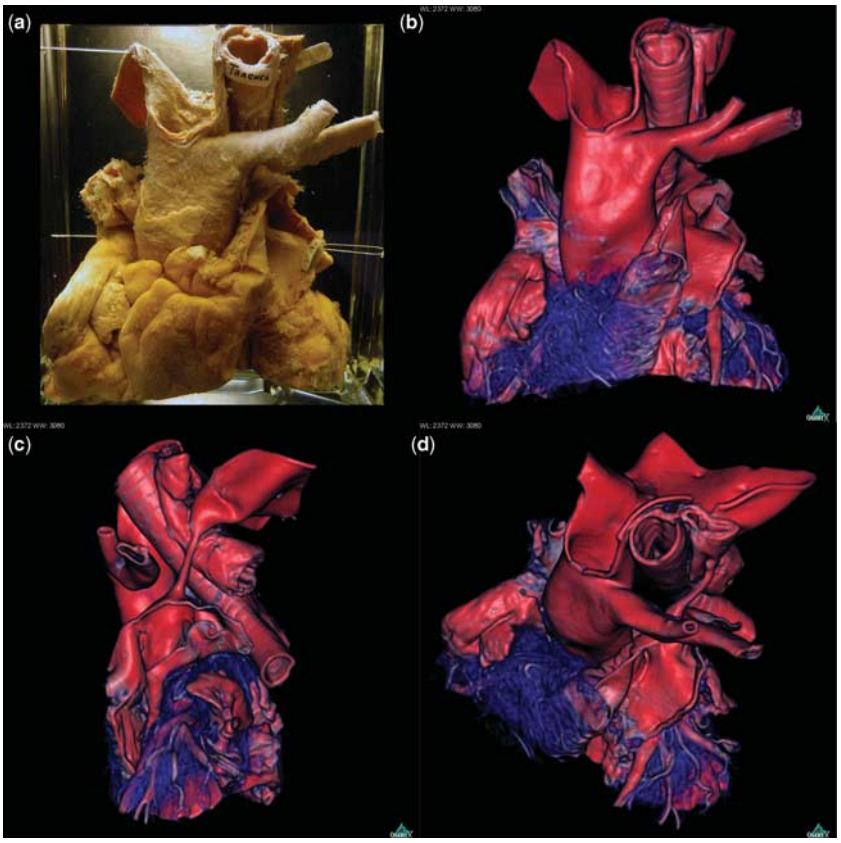

Figure 4.
*Specimen of vascular ring visible on the image (**a**) and its three-dimensional model shown in different projections on the images (**b–d**). The ductal ligament is clearly visible on image (**c**). The relationship between the vascular structures and the trachea is best displayed on images (**c, d**). Note how the coronary arteries hidden by the epicardial fat on the specimen, are clearly seen on the images (**b–d**).*

a 3-dimensional fast spoiled gradient recalled acquisition in the steady state; a 3D Fiesta sequence, a 3-dimensional balanced steady state free precession acquisitions; a 2D FSE T1, a 2-dimensional fast spin-echo T1 sequence; a 2D FSE T2 sequence, a 2-dimensional fast spin-echo T2 sequence; and the newer LAVA sequence, a 3-dimensional fast turbo gradient-echo sequence with T1 weighting (Fig 1). The BRAVO sequence, a fast inversion-recovery prepared 3-dimensional gradient-echo sequence, was tried on three of the smaller specimens (Fig 2).

The following table summarises the parameters used for the selected pulse sequences (Table 1).

The images were first processed on the Advantage Window version 4.2. The datasets were then transferred to a MacBook Pro laptop for final processing using the Osirix DICOM viewer available as freeware. The processing involved removing artefacts, and signal from the glass container, fluid media, and from matter in suspension. The specimens were examined by paging through individual images. We used multiplane reformatting to examine the specimens along, and perpendicular to structures of interest. We produced maximum intensity projection images and generated thick-slab renderings to get a better appreciation of volume and texture. Finally, we created textured virtual three-dimensional objects from which cutaway views could be made. Changes in colour mapping were made to alter perception of depth. The virtual objects were saved in DICOM, "QuickTime VR", and "QuickTime Fly-Thru" formats (Figs 4, 5, and 6).

Results

All specimens were successfully and easily scanned. None were damaged in the process. High-resolution three-dimensional and multi-planar-image processing was possible for all three-dimensional datasets. The best image quality, both for the native datasets and the quality of the reconstructions, was obtained by using a three-dimensional FSPGR pulse sequence in 4 to 7 minutes. Results with the BRAVO sequence, only available with the high definition eight-channel head coil, but done in less then 2 minutes, were nearly indistinguishable from the three-dimensional FSPGR (Figs 1 and 2).

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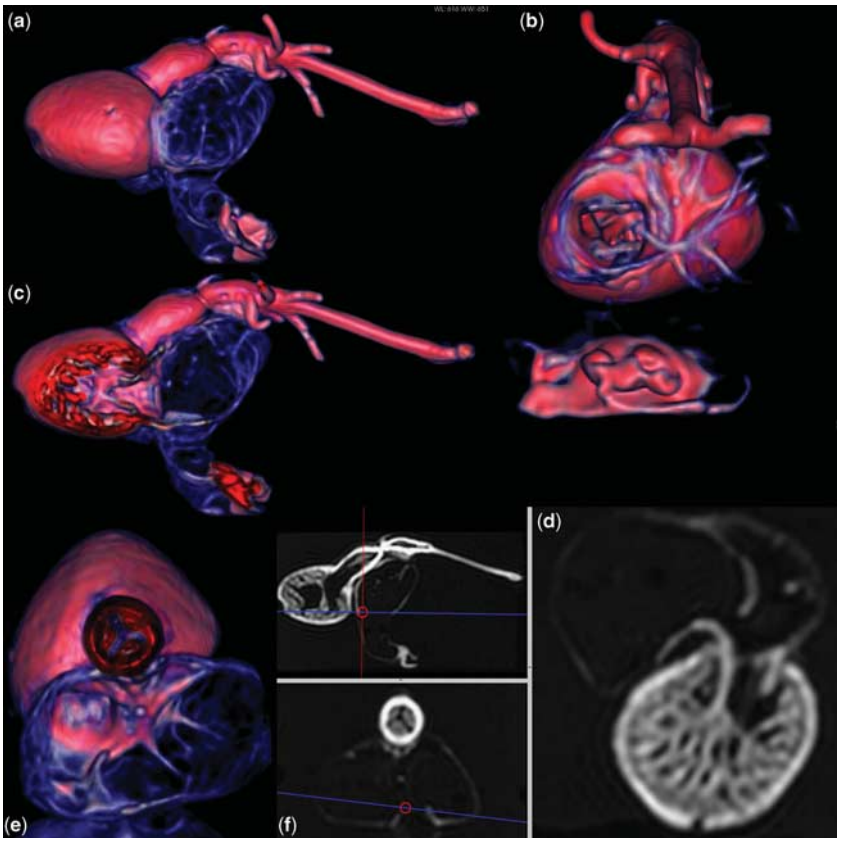

Figure 5.
*Multi-plane reformatting and three-dimensional rendering shown with cutaway views of a small shark heart (**a**–**f**). Note how multi-plane reformatting facilitates the examination of the specimen's internal structures (**f**, **d**), and allows the precise localisation of the aortic valve (**f**), the atrioventricular valve and atrial septum (**d**). This facilitates the creation of a cutaway virtual object that best shows the atrioventricular valve apparatus (**b**, **c**), and of the aortic valve (**e**).*

Technical notes

Image processing

The datasets were digitally manipulated to display surface anatomic characteristics of the specimens, as well as multiple concealed details (Figs 3, 4, and 5). Thick-slab renderings were created to depict the myocardial architecture (Fig 3b). Three-dimensional virtual specimens were created and examined from all angles (Fig 4). These virtual specimens were digitally dissected to reveal hidden parts of the anatomy (Figs 3c and 5). Changes in colour mapping were used to reveal superficial structures such as coronary arteries otherwise hidden under fatty layers (Fig 4b).

Pulse sequence selection and problem solving

T2 imaging is preferred for virtual pathology as it allows for greater tissue discrimination but makes the preservation fluid bright, because of the long T2 of water.[3,4] High signal makes it more difficult to separate the specimen from the media, while T1 imaging makes the specimen much brighter than the surrounding media. Inverting the grey scale helped as it made the fluid media appear dark on the T2 sequence (Fig 1b and 1c). As these specimens are already fixed, the need for greater tissue discrimination may not add as much information as it does in the examination of fresh specimens. The standard three-dimensional-FSPGR sequence and the newer three-dimensional-BRAVO sequence yielded the best results (Fig 2). The three-dimensional Fiesta, three-dimensional-LAVA, two-dimensional FSE T1, and two-dimensional FSE T2 sequences were not as successful in creating a noise free high-resolution dataset (Figs 1a, 1b, 1d, 1e, and 6b).

All metal appliances have to be removed prior to scanning as they produce large artefacts that in effect prevent imaging (Fig 6a).

The fluid media allows oscillation of the specimen due to the machine's vibrations during the scan. This results in a halo artefact around the specimen that may be difficult to edit digitally. The halo artefacts are the result of misregistration of spatial information in the phase encoding direction associated with movements of the subject; here, the

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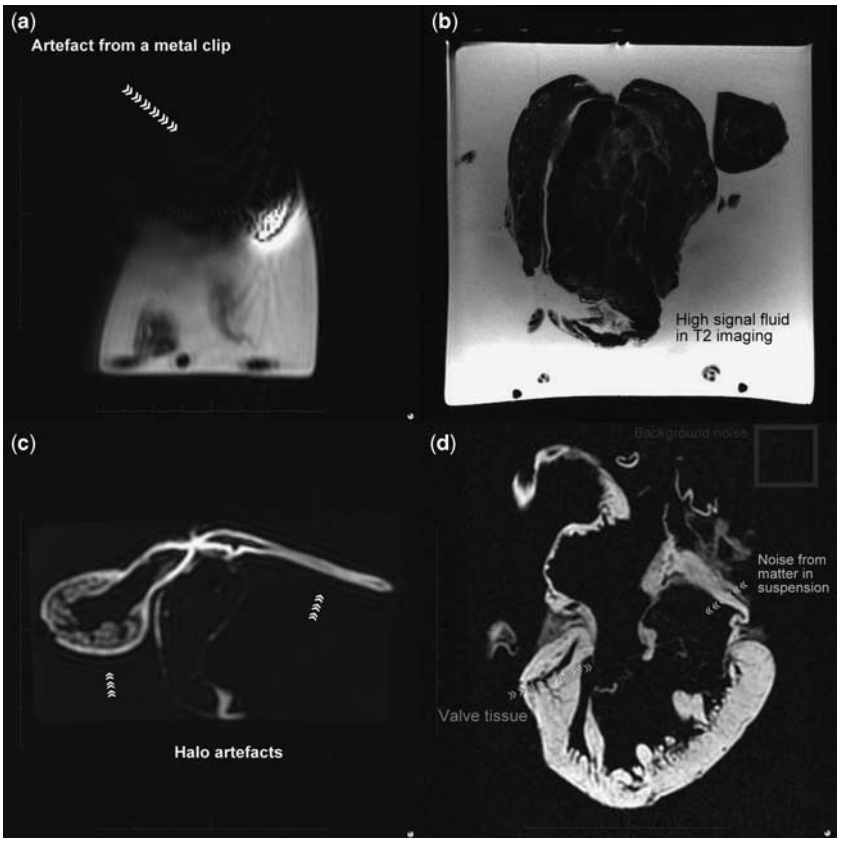

Figure 6.
*Examples of artefacts: (**a**) severe image distortion resulting from the presence of a metallic label stuck to one of the containers, (**b**) high signal of the surrounding fluid media with T2 imaging, (**c**) halo artefacts resulting from oscillation of the specimen in the fluid media, (**d**) background noise and noise resulting from the presence of matter in suspension that can interfere with three-dimensional rendering of more delicate structures such as the atrioventricular valves.*

specimen in the fluid media. We placed the specimens on a gel pad and secured them within the coil to reduce transmission of vibrations and minimise these halo artefacts (Fig 6c).

Signal from matter in suspension in the preservation solution and background noise could be edited out in most instances. Very delicate structures such as atrioventricular valve tissue, while easily identifiable on the native images and three-dimensional renderings, were difficult to separate from the surrounding media when trying to generate comprehensive three-dimensional reconstructions (Fig 6d).

Discussion

Pathologic specimens are prepared and preserved to provide insight into the structure, function, and embryology of the normal and congenitally abnormal heart. These have allowed thousands of physicians, researchers, and trainees their first opportunity to examine malformed hearts in detail.

For several reasons, it is becoming increasingly difficult to obtain and preserve new specimens, and as a result, growth of many collections has come to a halt. Meanwhile, the integrity of current collections is destined to degrade because of the inherent fragility of the pathological specimens.

Over the years, several strategies have been elaborated to extend the life of heart specimens, while trying to keep them available for study. For the Maude Abbott collection, the specimens were suspended in Kaiserling III solution after have been dissected and mounted with interesting parts of the anatomy exposed. They were sealed in a clear glass container for viewing. This preservation technique slowed down the degradation of the specimen but created a physical barrier limiting its examination. Unfortunately, the pre-dissection and displaying process would often distort the anatomic relationships expected in these anatomically abnormal hearts. In addition, although some interesting parts of the cardiac anatomy would be exposed, others would remain hidden to the viewer.

The digitisation of specimens can create a permanent record of congenitally abnormal hearts. The resulting images can be manipulated to gain

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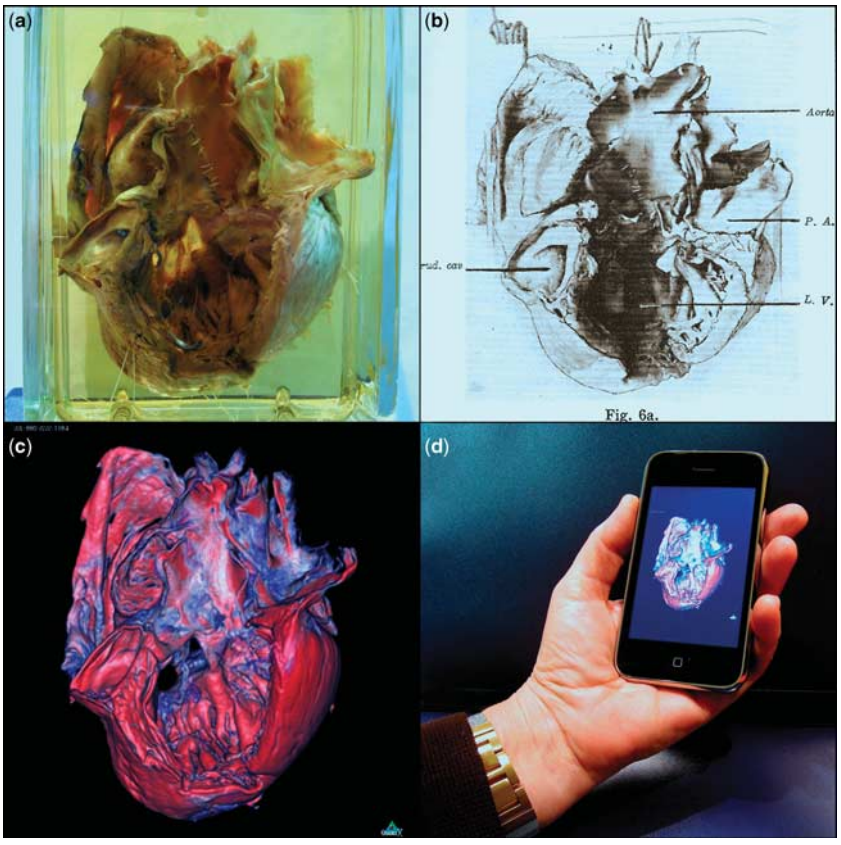

Figure 7.
*The original "Holmes Heart" of 1823 in its glass container (**a**), drawn and described in detail in Maude Abbott's famous Atlas published in 1936 (**b**), made into a digital object (**c**) sent to a portable phone in 2009 (**d**).*

detailed knowledge by examination of the source images or by the creation of sophisticated three-dimensional rendering without physically touching these fragile specimens. These virtual objects can also be given substance by using techniques such as "rapid prototyping", a technique that creates objects from acrylonitrile butadiene styrene polymer powders.[6,7] High-resolution magnetic-resonance imaging and computerised tomography are obvious choices when attempting to create a digital library of pathological specimens. We chose magnetic-resonance imaging as it combined high-resolution imaging with an inherent ability for tissue discrimination.

These techniques could not only allow the creation of a permanent record for historical collections, but may also allow for future growth of these collections; as the hearts, once imaged, may be returned to their families. The International Society for Nomenclature of Paediatric and Congenital Heart Disease has founded a working group for archiving and cataloguing of cardiac images and videos. Through the use of magnetic-resonance imaging of historical specimens, the working group's digital repository can potentially contain a wealth of material previously inaccessible to most students of paediatric and congenital cardiac disease, thereby fulfilling a mandate to preserve the legacy of historical pathological specimens. These digital records can easily be made available to students, physicians, and researchers throughout the world via the web (Fig 7).

Pathological specimens can successfully be scanned in minutes resulting in unalterable and portable high-resolution three-dimensional datasets that can be processed by using inexpensive and readily available software. The resulting images can also be used for viewing by untrained individuals. Magnetic-resonance imaging of pathological specimens could ensure continued access to hearts for teaching and scientific purposes, and further our understanding of the congenitally malformed heart.

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