Method Article

Modelling and fabrication procedure for a 3D printed cardiac model - surgical planning of Left Ventricular Aneurysm✩

Francesco Buonamici a,∗, Elisa Mussi a, Chiara Santarelli a, Nazario Carrabba b, Pierluigi Stefano b, Niccolò Marchionni b, Monica Carfagni a

a Department of industrial Engineering of Florence, Italy
b Department Cardiothoracovascular, Careggi Hospital, Italy

ABSTRACT

The present paper describes a procedure for the development and production of a physical model for surgical planning of a Left Ventricular Aneurysm. The method is based on the general approach provided in Otton et al. (2017) and was customized to seek a reliable and fast procedure for the production of a specific type of cardiac model – i.e. chambers of the left side of the heart. The paper covers all the steps: processing of the data, segmentation, modelling and 3D printing; details are provided for all the phases, in order to allow the reproduction of the achieved results. The procedure relies on Computed Tomography - CT imaging as data source for the identification and modelling of the anatomy. Materialise Mimics was used as segmentation software to process the CT data. While its usefulness for the surgical needs was verified on a single clinical case (provided by the Careggi Hospital of Florence, Italy), the modelling procedure was tested twice, to produce a physical replica both ex-ante and ex-post surgical intervention.

• The tools used for segmentation and generation of the printable model were customized to reduce modelling time for the specific type of desired model.
• Detailed information on the use of modeling tools, not available in the literature, will be provided.
• The procedure allows fabrication of a physical model representing the heart chambers in a short time.

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✩ Direct Submission or Co-Submission: Direct Submission.
∗ Corresponding author.
E-mail address: Francesco.buonamici@unifi.it (F. Buonamici).

https://doi.org/10.1016/j.mex.2022.101822
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Specifications table

| Subject area: | Engineering |
|---------------|-------------|
| More specific subject area: | CAD Anatomical Modeling & 3D Printing |
| Method name: | Method for the production of an anatomical replica of a human heart for surgical planning |
| Name and reference of original method: | Otton JM, Birbara NS, Hussain T, Greil G, Foley TA, Pather N. 3D printing from cardiovascular CT: a practical guide and review. Cardiovasc Diagn Ther. 2017 Oct;7(5):507–526. doi: 10.21037/cdt.2017.01.12. PMID: 29,255,693; PMCID: PMC5716949. |
| Resource availability: | Segmentation software: Materialise Mimics 23 |
| | https://www.materialise.com/en/medical/mimics-innovation-suite/mimics |
| | FFF Printer: Cura 3D printing software |
| | https://ultimaker.com/it/software/ultimaker-cura or Makerbot Replicator Plus |
| | https://www.makerbot.com/it/3d-printers/replicator/ |
| | PLA Material for Makerbot Replicator Plus: |
| | https://store.makerbot.com/3d-printers-materials/replicator-spool/pla-large |
| | Makerbot Replicator Plus print software: |
| | https://www.makerbot.com/it/3d-printers/apps/makerbot-print/ |

Method details

**Background**

3D printing allows for a rapid production of digital models. The recent expansion of this class of technologies and the vast commercialization of affordable and easy-to-use systems has made their application possible in a wide variety of areas. A significative example is the fabrication of anatomical replicas, task trainers and simulators that are used by surgeons in the planning phase of an intervention. 3D printing technologies offer significative advantages for this application, as they allow the fabrication of complex parts, in small batches or even in single units, with little-to-none setup time (nevertheless, a considerable time is required by the manufacturing process itself). Time is a fundamental aspect, especially facing an emergency surgery that could benefit from the development of a 3D model for planning during the preparation phase. In such cases, the available time window for the fabrication of the device is severely limited.

The time required to obtain a physical copy of the specific anatomy of the patients – i.e. a personalized 3D model – highly depends on the complexity of the anatomy and on the characteristics of the model. Highly advanced simulators, which make use of tissue-mimicking materials, evidently require a refined process both in the modeling and fabrication phases. The major factor influencing manufacture times is the type of process selected: additive technologies are known for their modest build rate which can penalize the fabrication of large parts. In this context, the choice of a specific additive process could further penalize or mitigate manufacturing times. Furthermore, whenever additional processes (e.g. silicon casting, coating, subtractive processes) need to be integrated, fabrication times significantly grow. These elements directly depend on the properties and functionalities required from the device; accordingly, designers usually have limited scope for action to reduce fabrication times, mainly by tweaking of process parameters.

On the other hand, the modeling phase – i.e. the series of operations leading from the information contained in the diagnostic images to the digital model of the device ready to be printed – presents a high margin of improvement. While the main workflow is established, multiple tools and strategies can be used depending on (i) the anatomy of interest, (ii) the type of physical device that need to be produced and (iii) the experience of the designer. As a result, the literature does not offer
any precise methods, procedures and guidelines to be followed. This article presents a method for the achievement of a digital cardiac model composed of a set of chambers of the heart starting from a contrast enhanced Computer Tomography – CT in a timely and efficient way. The process is defined with the aim of producing a physical device reproducing the shape of the blood pools of two chambers (Atrium – A, Ventricle – V). The process can be adapted with little effort for the production of a model of the left/right chambers of the heart (Left Ventricle - LV, Right Ventricle - RV, Left Atrium - LA, Right Atrium - RA); most notable differences, in such case, will be faced in the type of diagnostic image that should be assured to start the process and, with respect to the modeling phase, to the correct identification of valves. The discussed method refers to the general approach presented in [1]. The authors of [1] provide a series of considerations and advices to perform the segmentation of a generic cardiac model starting from CT data. The present article customizes it through all the steps with specific choices made for the sake of efficiency. The procedure considers both the modeling phase and the preparation of the 3D printing process using a Fused Filament Fabrication - FFF machine. As previously mentioned, the overall time required for the production of a final 3D printed model is of crucial importance; research efforts are therefore required to improve this specific parameter. The procedure makes use of Materialise Mimics® 23 as software package of choice to perform the central steps of the methodology (i.e. the generation of digital models representing the anatomy of interest). Several software packages, capable of reading CT data and offering tools to perform segmentation and modeling tasks, ultimately leading to the generation of a digital 3D model of the anatomy of interest, do exist. Most renown commercial packages are arguably Materialise Mimics®, Synopsys Simpleware®, 3D Slicer, 3D Systems D2P; all these systems offer tools to perform semi-automatic segmentation tasks. Some differences can be found in the performances, especially considering the automation level of the tools (Stratasys DLP is focused on this aspect), with Mimics offering a more complete suite of tools. All the software previously mentioned offer an environment capable of hosting the procedure hereby described. Slight changes to the application of the specific steps could be required depending on the software of choice. For the interested reader, a review of segmentation software packages is presented in [2].

The procedure

The modeling procedure starts with the information provided by the diagnostic image of the patient. This method, as previously mentioned, considers the case of CT data as starting point. We propose the workflow depicted in Fig. 1. In the figure, each step is reported with major choices that need to be made. The workflow is derived directly from the general procedure presented in [1], suitably adapted to this application. Moreover, the figure provides a general indication regarding the approximate time that each step should require considering the scenario of a limited time window to obtain the final printed model. The time values evidently depend on multiple factors: specific anatomy of the patient, quality of the CT data, experience of the user; accordingly, they should be considered only as general indications. The reader interested in reproducing the method should consider them mainly to calibrate the resources that should be spent on each step in order to maximize the quality of the model given a limited time window. A valid management of the time resources available to the person/team responsible for the creation of the printed anatomical model is one of the most important results that this procedure seeks. While hardware resources, both in terms of computational power and 3D printing machine available by a possible future are evidently important factors influencing the overall delivery time, time spent for manual operations by the user in charge of the process remain the most impacting one. Accordingly, this procedure aims at optimizing the workflow followed by the user, hence improving the overall process in a noticeable way. A proper formalization of the suggested workflow to produce cardiac models of the hearth chambers is a valid contribution to the literature, which lacks in procedures that could help clinical engineers assisting surgeons with the development and production of anatomical reference models. Specifically, this procedure could allow a reduction of the risks that originate trying to develop a custom workflow.

In the following, each step of the method will be discussed in depth. The description will provide general (i.e. valid for the generation of any cardiac model) as well as specific indications, valid
Fig. 1. Procedure workflow. Rough estimates of the time required to complete each task.

for the specific case of models whom Region Of Interest - ROI is limited to atrium and ventricle chambers. This type of model, describing the shape of the heart blood pools, is useful in the planning phases of surgical interventions where the goal is reshaping the LV/RV: such operations aim at the reconstruction of a functioning ventricle by operating on the ventricle cardiac muscles. Accordingly, a complete understanding of the three-dimensional shape of the heart cavity, as well as of the relative positions and dimensions of all the principal cardiac structures of the patient can enormously improve the quality of the intervention, especially in terms of execution time. This type of operation often requires a prompt response from the surgical team, who has little time to prepare the intervention; accordingly, the production of any model to aid the surgeon needs to be performed in a short time and efficiently, with a minimal margin for errors. This justifies the development of a dedicated
procedure. The procedure was tested for the production of a LV/LA 3D printed model for a case of LV Aneurysm (LVA) that was treated surgically with a complete reshaping of the LV. The application of the procedure is described in the final section of the paper.

Step 1 - Hospital acquisition protocol

The acquisition protocol to obtain the diagnostic image used to guide the modeling of the device is the first step of the process that should be examined. The protocol includes all the hardware and acquisition parameters used by the hospital. While the type of CT system used for the acquisition is generally a constraint imposed by the available resources, acquisition parameters can be tailored, as well as the mode of administering contrast agents.

A change in the acquisition parameters, especially in the timing used for contrast detection and in the slice thickness, can cause a significant change in the resulting medical data. With this respect, a thinner slice is always desirable as it allows the description of anatomical structure with a higher resolution; redundant data, whenever it is not required, can always be discarded (e.g. by not considering a series of slices) to reduce processing times.

Moreover, a fundamental step is the following generation of the reconstructed images, which is performed on-board of the scanner by several algorithms. This problem is studied and described in the literature [3]. The authors highlight the importance of studying and choosing the effects of different kernels in CT scanning depending on the type of result that is required. Although the case study described in the paper only involves bone tissue, the considerations moved by the authors have general validity.

In the method described in the present paper, a contrast-enhanced CT scan with high pitch and dual source, obtained using retrospective ECG-gated (controlled by an ElectroCardioGram - ECG) spiral acquisition and tube modulation was used. The contrast allowed to highlight left chambers of the heart of the patient, thanks to a higher contrast visible in the medical images, facilitating the subsequent segmentation and the general identification of the structures for diagnostic needs. Cardiac CTs are often performed even without contrast administration; in such cases the identification of the specifics of the ROI to be printed could be hindered, but still possible, depending on the needs of the medical team. Indeed, gated images are essential to assure that small structures are correctly represented and to acquire high-fidelity measures.

It is important to note that in most cases the CT data used to build a 3D anatomical model is not obtained in a dedicated exam, tailored to maximize the quality of the reconstruction. Typically, diagnostic images were acquired with a different goal and, accordingly, should be always checked at the start of the reconstruction to assure that the quality is sufficient. Main aspects that should be considered are:

- Slice thickness sufficiently thin; no major anatomes structures should be filtered out. 0.3 mm are ideal for cardiac modeling but lower resolutions can be acceptable.
- Presence of artefacts due to external structures interfering with anatomies of interest (e.g. pacemaker)
- Sufficient contrast in the area of interest

With this respect, it is impossible to define specific values for some parameters, as the quality of the model is directly correlated to the medical needs. When the exam is specifically performed for 3D printing purposes, the best parameters to assure high quality would require the choice of higher mA/kV (depending on patient body), which minimize signal to noise levels. Occasionally, the accentuation of vessel and blood pools can be obtained with Low kV CT imaging by calibrating the amount of injected contrast [1].

Step 2 - RAW segmentation guided by radiologist or medic

This steps clearly identifies the clinical indications that are required to assure the efficacy of the printed device; such indications should result directly from the clinical question that has brought to the activation of the entire modeling/printing workflow for the specific case considered. The workflow presented in the paper considers the hypothesis of a user, responsible for the modeling/printing phases, who is distinct from the medical personnel that has clinical interest in the production of a 3D printed model. This is a real-case scenario, as segmentation, modeling and 3D printing are typically assigned to engineers who have an in-depth knowledge on technical tools but lack the
expertise required to comprehend all the medical aspects of the case and, more importantly, cannot take full responsibility for the production of a medical device that could influence the result of a clinical decision.

Accordingly, a first discussion between medics and engineers is mandatory for the correct identification of the ROI and to define the constraints to be observed. Quality management cannot be overlooked in favor of a reduction of production times; the definition of a set of constraints that must be observed during the procedure and that can be checked at the end is important.

The person responsible for the production of the model should study the diagnostic exam in a preliminary phase starting from a rough description of the case that should be provided by the medical team. Main doubts and possible complications should be identified prior to the Step 2 itself in order to improve communication and assure that all the technical aspects are covered.

During this discussion, the following points should be addressed:

- Phase of the cardiac cycle selected for the production of the model.
- General ROI – definition of the volumes/tissues/regions of interest for the specific case. The fundamental information is the identification of the heart chambers to be printed.
- Specific ROI - On a second level, the medic should identify the areas of special interest for them. Notable examples are: region that will be treated during surgery (tissues, anatomical structures), level of definition of the cardiovascular system (which vases should be represented, to what extent), level of definition of the valve apparatus (e.g. Mitral and Aortic Valve for LV/AV models, etc.).
- Available time resources
- Raw Segmentation – While the segmentation of the previously mentioned General ROI could be performed almost automatically, the correct identification of the regions of special interest should be guided by someone with specific knowledge on the case treated and with medical training.

All the details emerged during the meeting will go into a technical specification that will remain available as reference during the entire workflow. The last step – i.e. raw segmentation - is performed directly within an imaging software, analyzing the CT and introducing markers, annotations and starting the segmentation activity. This procedure makes use of Materialise Mimics® 23, a medical imaging software which offers tools to perform segmentation and 3D modeling of anatomical models. Specifically, Mimics® offers the following tools which proved to be really useful for this step:

- Text annotations
- Point-to-point distance
- Segmentation masks
- Spline creation

These tools are used to introduce fixed reference points and structures on the patient CT together with the medic. It is important to highlight that annotation tools which allow the user to link a piece of information with a specific 3D point or region on the medical image are offered in every package. Such indications are fundamental to allow the engineering team to continue the procedure independently, maximizing its efficiency.

Text annotations and splines are used to identify heart landmarks that could guide the segmentation. Minor veins and arteries that need to be represented should be identified (e.g. coronaries) as well as distal limits to stop segmentation of vases that communicate with the principal heart chambers. Other landmarks that should be identified are: papillary muscles limits (insertion of chordae, connection point with the pericardium), Interventricular septum, fossa ovalis, main volumes of the auricles to be represented in case of complex anatomies, valve flaps and coaptation profile etc.

Segmentation masks created in this phase can further guide the subsequent work but their generation is a far slower process; accordingly, they should be used only to trace the shape of interfaces and structures that are difficult to read from the CT and that should be read in the light of a deep anatomical knowledge. In such cases, manual segmentation tools (e.g. paintbrush guided by the user) are the only kind of tools applicable for this purpose.

Complex situations can be resolved recurring to additional data obtained from other diagnostic images. While the introduction of fusion techniques, capable of integrating the data obtained from
MRIs and Uls significantly slow down the process, such data can be used to acquire knowledge on the anatomies to be segmented and use it to guide the segmentation of the CT data. 4D data is usually extremely useful in this context as well, as it can highlight the shape of the structure to be segmented on the frame of interest. Whenever required, additional imaging can be integrated with the CT data: subsequent phases of the workflow are applied on the integrated data without any substantial change.  

Step 3 - Filtering  

Filters are often applied to CT data to improve readability and usability of the diagnostic data. Obviously, every modification to the original data should be introduced with care and the unfiltered data should always be kept available to double-check the segmentation results.  

Filters are mainly applied to denoise the original image, allowing a clear identification of the structures of interest. To better explain the importance of filtering in the context of 3D printing of cardiac models, the strategies used to segment the ROIs need to be introduced. Segmentation can be performed relying on semi-automatic tools or on manual techniques. Manual techniques require a user highly skilled in the identification of the structures; when a purely manual workflow is applied, the efforts required to complete it are only dependant on the user manual dexterity. Automatic tools offered by imaging software, on the other hand, rely on the analysis of Hounsfield unit levels and their distribution to group areas with similar grey levels that could belong to the same anatomical structure.  

Filters may help in uniformizing grey pools, obtaining larger volumes with similar grey levels. Moreover, filters can be applied quickly to the entire set of images, without the need for “local” operations. While a general loss of details is usually observed when applying denoising filters, the demarcation of large volumes such as cardiac blood pools becomes more pronounced. Accordingly, heart chambers, specifically, can be easily segmented (i.e. isolated with a reduced number of manual operations) even though with lesser details on the borders. Filters that fall in this class and that can be applied to pursue this goal are: median filters, mean filters, curvature flow filters, denoising filters (speckle removal, grain removal).  

Another result that can be pursued using specific filters is the enhancement of the available data to better guide the segmentation performed using manual tools. Filters capable of highlighting borders like gradient magnitude filters (Fig. 2d) are particularly useful and can be applied for this purpose.  

The procedure presented in this paper makes use of two different filters to obtain digital copies of the original exam to be used to speed up the segmentation and modeling phases. The first filter is a curvature flow to the entire CT to process the data to be used for automatic segmentation of the less-important areas. Curvature flow filter details can be found in Table 1. The second one is a gradient magnitude: its result can be used as reference data to provide more information to the person responsible for the manual segmentation. Its effects are visible in Fig. 2d.  

Step 4 - Segmentation  

Segmentation takes filtered and unfiltered images in input to produce masks that isolate and label different anatomical structures across each slice of the CT data. Such masks can later be used to reconstruct proper 3D models by triangulating the external surfaces of the identified regions. This procedure proposes a segmentation process based on two parallel paths, working on both filtered and unfiltered images. These processes will be called “fast” and “precise” in the following paragraphs.  

As previously mentioned, some classes of filtered images are more suitable to apply automatic segmentation procedures, as they have a general effect of uniformization of grey levels and the consequent generation of cleaner and more regular Hounsfield unit isocontours. This comes at the cost of a loss of resolution and details. While this tradeoff is evidently not acceptable in the ROI of the CT data or, in general, where the reconstruction of the thin and detailed structures needs to be.

| Table 1 | Curvature flow filter details. |
|---------|-------------------------------|
| Time step | 0.5 |
| Number of Iterations | 6 |
performed, significant advantages can be obtained for the reconstruction of the less-important areas of the model.

Clinical indications, obtained in the raw segmentation step, are exploited in this phase to guide the process. Annotations, measures, and first-attempt masks are used to reduce the probability of errors. Specifically, clinical indications are used to identify the CT regions that need to be segmented with the highest accuracy possible and which regions can be addressed with the fast route. The user should take into account ROI indications, specific surgical conditions that will be faced by the surgeon, defective or anormal anatomies or strange behaviors of the contrast agent which can alter the expected result.

Once that these areas are identified, the segmentation proceeds on parallel tracks. This procedure uses Materialise Mimics 23® for the segmentation, but other similar software packages which offer interactive segmentation tools can be used. As previously mentioned, this procedure aims at the generation of a 3D replica of the heart chambers; accordingly, the aim of the segmentation is the isolation of all the volumes occupied by the blood (i.e. blood pools). Contrast-enhanced cardiac CT highlight blood pools: such areas are lighten up by the contrast liquid. Accordingly, contrast-enhanced regions are characterized by grey levels closer to white, with a higher brightness. In the following paragraphs, a short introduction on the best practice that the present procedure advises for the segmentation of different anatomical structures of the heart, is presented.

The segmentation of main vessels (aorta AO, superior vena cava SVC, inferior vena cava IVC, pulmonary artery PA) that are in communication with the heart chambers is usually straightforward. Such structures are characterized by a recognizable elliptical or circular section that is visible on one of the principal plans, which eases the segmentation process. Moreover, clinical requirements are usually directed towards main chambers (LV, LA, RV, RA) and segmentation of the AO, SVC, IVC, PA can be performed with less accuracy. Such structures are often removed partially or entirely from the printed models: their thin structures and elongated shapes greatly complicate the printing process and whenever possible, they should be removed to save printing time and avoid complications.

Fig. 2. Effect of different filters applied to a cardiac CT: (a) original image of the LV in sagittal view (papillary muscles region) (b) filtered image with a median filter applied in a 5 px area; (c) original image of the LA/LV chambers in axial view; (d) filtered image with a gradient magnitude filter applied.
The atria, with the exception of the auricles (Left Atrial Auricle - LAA, Right Atrial Auricle - RAA), are characterized by an internal surface that is quite smooth and regular; for this reason, first-attempt segmentation results that can be obtained with automatic tools can be easily improved with the help of smoothing operations. Ventricles, on the other hand, present an internal structure far more complicated: pectinate muscles define a rough and textured surface that, depending on the CT characteristics, can obstacle the identification of a well-defined border; moreover, papillary muscles extend from the surface to the centre of the ventricle, complicating the boundary identification process.

Finally, special attention should be given to specific structures that are either very important for the clinical needs (i.e. specific area of intervention) or too small/detailed to be easily segmented; notable examples are the valves (Mitral Valve - MV, Aortic Valve - AV, Pulmonic Valve - PV, Tricuspid Valve - TV) and the left and right auricles (LAA, RAA). Such elements, especially the valves, are only partially represented with a CT acquisition and their reconstruction needs to be performed manually, integrating the poor visual details presented in the exam with a deep anatomical knowledge.

Procedurally, the choice between fast and precise approaches and accordingly between filtered images or original images should be taken considering the anatomy to be segmented, the clinical interest and the specific quality of the CT data available. The presented approach advise for the creation of multiple segmentation masks to be integrated at the end of the segmentation process. Such masks are fused together using Boolean functions and they should be built assuring that precise and fast masks do not overlap in the regions that require a precise segmentation. Conversely, a good overlap should be researched in the less important areas to avoid hole formation during the fuse process. In other words, precise masks should extend outside the areas designated to be segmented with such approach. All the created masks should be saved at various stages in order to account for possible mistakes or to use them later in the process in combination with other masks by means of Boolean Operations.

**Fast approach - filtered images**

This process mainly exploits automatic tools provided by the segmentation software. This approach should be applied preferably to the following structures: LA, RA, AO, SVC, IVC, SVC, PA. Moreover, it can be applied to LV and RV chambers in areas that are not particularly important. Most useful tools that can be used within Materialise Mimics® to pursue the fast approach are reported in the following text, with a brief description of its functioning and their application to the considered scenario.

- **Threshold** – It is one of the tools applied at the start of the segmentation process. Threshold selects all the pixels contained within a selected bounding box that fall in a pre-determined intensity range. The result is a rough mask which typically requires refinement with additional tools.

- **Multiple Slice Edit** – It works on one of the principal views of the CT performing an interpolation of masks drawn on a limited number of slices; the user produces a segmentation of most important slices and obtains, as a result, a mask for each section included in the selected interval. The tool can be used in combination with a threshold definition, which constraints the interpolation to the selection of pixel in a specified intensity range. It is particularly useful for the segmentation of structures that have a recognizable and “clean” section on one of the three principal plains which evolves with limited variations navigating through the slices. This way, a large segmentation mask can be obtained with limited errors starting with few manually-built slices. The elective

- **Region Grow** – Starting from the selection of a seed pixel (or a series of seeds), it isolates single parts of a pre-built mask performing a connectivity analysis. It is useful to perform a first refinement of a mask obtained through threshold to eliminate isolated parts. It can be applied to isolate major LV/LA RV/RA volumes and the connected vascular system.

- **Dynamic Region Grow** – Performs an operation similar to Region Grow but takes in input multiple seed points across multiple layers; hence, different grey levels can be used to better control the connectivity analysis; moreover, threshold values on the similarity of grey levels and expansion of the resulting mask can be applied. This is particularly useful when the simple Region Grow produces unsatisfactory results. Moreover, it is applied when the effect caused by the contrast agent
significant varies across the blood pool to be segmented. It can be used to produce valid starting points for the segmentation of main chambers.

- **3D Interpolate** – It performs an interpolation similar to Multiple Slice Edit but exploiting seed masks generated on every principal anatomical plain. This is useful for structures whose shape cannot be described using a single perspective. As an example, the LA/RA and LV/RV shapes can be obtained with this approach. Ventricle volumes, due to their more complex shape, can benefit from this approach; see Fig. 3 for a significant example.

- **Smart Fill** – this function analyses an input mask and fills a series of holes (groups of inactive pixels that are partially or totally enclosed within a mask). The size of the maximum holes filled is controlled by selecting the number of voxels.

Furthermore, Materialise Mimics® offer a high-automation tool dedicated to the segmentation of the major heart blood pools. The tool is called CT Heart and performs a semi-automatic segmentation of all the internal volumes of the heart starting from seed points provided by the user through a point and click process and threshold range. Ideally, the user needs only to label principal areas of the heart navigating the CT data (LV, RV, LA, RA, AO, PA). The software performs an automatic segmentation evaluating the CT Haunsfield units and provides a series of masks (Fig. 4). The quality of the result depends mainly on the difference in brightness between the blood and surrounding structures of the heart: highly contrasted areas are clearly segmented while significant errors arise in presence of less defined borders. Nevertheless, a first attempt to perform this kind of automatic segmentation can be performed: obtained results should be carefully evaluated to select useful segmentation masks that can be eventually integrated using the procedure presented in the following text.

3D Slicer offers a similar tool, which can be applied to isolate different regions in an automatic fashion (i.e. “Grow from seeds”); its application on the identification of the main chambers of the heart produces similar results.

The present procedure relies on the framework summarized in Table 2, which needs to be personalized depending on the specific needs. The steps are presented in the table in chronological order. Steps 3–6 should be considered depending on the results obtained in Task 1. The results obtained at each step should be checked to avoid the emergence of undesirable effects. Most of the tools reported in Table 2 implement a semi-automatic segmentation approach; nevertheless, manual interventions are still required in certain parts of the fast procedure (for example to remove macro areas from the resulting segmentation mask, as showed in Fig. 5). Different names could be used across different software packages to indicate the type of tool described in the table. The nomenclature used refers to Materialise Mimics®.
### Table 2

**Fast segmentation workflow.**

| Step | Tool | Description/Addressed areas |
|------|------|-----------------------------|
| 1    | CT Heart | First attempt is dedicated to an automatic segmentation of the entire heart through the use of the CT heart tool offered in the “Advanced segmentation” tab. If the results are not satisfactory, Step 2 can be used as starting point of the procedure. |
| 2    | Threshold | Select a bounding box that includes the entire heart. If only one side (left/right) needs to be segmented, the bounding box should be further reduced. Manual selection of a valid threshold value, which includes all the pixel that can be attributed to the blood and exclude the others. A perfect selection is not possible, as there always be some pixel highlighted in the surrounding tissue and some missing pixels in the blood pools. When facing this issue, preference should be given to the creation of well separated masks, accepting the presence of several missing pixel inside the blood pools. Such defects can be easily fixed later, while the fuse of different blood pools is a problem that requires intense manual work to be addressed. See Fig. 6 and Fig. 7 for a practical example. |
| 3    | Region Grow / Dynamic Region Grow | Fast cleaning of the results obtained at the step 3. Region grow is applied clicking on one of the main blood pools to remove every isolated group of pixel. Dynamic region grow is subsequently applied to further refine the area of interest to a series of masks. First attempts, later integrated in step 5, can be performed to separate LV, RV, LA, RA, AO, PA, IVC. |
| 4    | Edit mask (lasso tool to remove areas) | Evaluation of the result obtained with the CT Heart tool. Manual removal of areas that are not included in the model, for example the derivations of the cardiovascular system (Fig. 5). Large volumes can be effectively removed by separating them from the useful part of the mask in two steps: (i) working directly on the 3D mask by removing small areas at the border of the useful mask with the lasso tool and (ii) completely remove the detached part applying the Region Grow tool. Moreover, the user should remove areas that will be segmented with the precise approach from the obtained fast masks, in order to remove overlays and guarantee the integrity of the precise ones. Mask quality control should be focused in the MV AV PV TV areas, especially to check the correct separation between atria and ventricles. As previously discussed, manual refinements are usually required in such areas. |
| 5    | Manual Tools | Separation of the main blood pools that are fused together at the end of Step 4 (LV, RV, LA, RA, AO, PA, IVC, SVC). The separation is required even if the procedure requires the generation of a single mask at the end. This is to allow the user to work independently on each mask with the most suitable tools without influencing the other parts. A rough separation can be performed practically in every case with the use of lasso tool. Main arteries and veins can be reconstructed using the Multiple Slice Edit tool (Step 5) so the raw segmentation provided by step 3 for such areas is useful only in rare cases. The Split Masks tool can be alternatively applied for this purpose. Ventricles and atria separations should be performed trying to follow the plane of the valves that separate them but taking into consideration that such areas will be addressed with the precise approach and, ultimately, integrated. |
| 6    | Multiple Slice Edit | Reconstruction of main arteries/veins exploiting their recognizable elliptic/circular shape on the sectional planes using the Multiple Slice Edit (MSE) tool. LA and RA masks can be further edited, if required, with the MSE tool to improve the segmentation at the borders and in the areas where the contrast is dim. LAA and RAA are segmented with the precise approach. |
| 7    | Smart Fill | Holes filling for separated masks. The tool is progressively applied increasing the number of voxels (1, 2, 3, etc.). At each step the user should check the result and eventually undo the last application of the tool whenever negative results are observed. |
| 8    | Smooth | Smoothing operations to improve the regularity of the borders of the segmentation mask. It can be applied multiple times on regular volumes and with caution to more jagged masks. |
| 9    | Final result | LV/LA or RV/RA main volumes (depending on the clinical interest). Additional volumes for AO PA IVC SVC whenever required for additional evaluation. |
| Alternative 3D interpolate to steps 2/6 | | Creation of LV RV masks that could offer better results compared with those obtained at the end of step 7. Manual segmentation of most significative planes for LV and RV volumes. |
Precise approach – unfiltered images

This part of the procedure mainly exploits manual tools that are applied by the user to generate a set of masks by intentionally selecting each pixel. This workflow is more time-consuming but allows a complete control on the definition of the segmentation masks. Moreover, its efficiency is entirely dependent to the experience and skills of the user in charge of the process. This procedure advises the use of a graphics tablet which, due to the type of tools typically offered by medical segmentation software packages, can speed up the “painting” process of the analyzed structures. The main tools used in this process are the Edit mask tool and the Multiple Slice Edit tool. Both allow the selection of pixel on the CT slices by means of different kind of user interaction: painting with a digital brush, windowing, selecting group of pixels with similar intensity (point and click). Depending on the size and type of anatomical structure, the workflow can start from the masks obtained from the step 1 and 2 of the fast procedure, which can be corrected and improved. Usually this is convenient when
Fig. 6. Segmentation performed using the threshold tool. Different results obtained using a correct intensity range (yellow) and a range too wide (blue), which causes the introduction of noise and connected structures in the resulting masks.

Fig. 7. Segmentation error typically resulting from a too wide intensity range: AO and PA volumes are touching in the zoomed area. This can cause problems in subsequent phases.

working with large volumes, which would require significant times to be processed entirely manually. Whenever border enhancing filters were applied during the filtering step, the obtained data can be used as reference. Alternatively, the process can start directly from the unfiltered data which can be used to paint manual masks.

In other cases, it is easier to work with “negative masks”, selecting pixels that should not be part of the final result and later subtracting them from raw masks to obtain a refined result; see Fig. 8 for an example.

Manual interventions are always required in the LAA, RAA, MV, AV, PV, TV areas. Such areas are limited in space and, due to the complexity and dimensions of the structures involved, they should always be manually segmented. Obtained results should be thoroughly checked during the final segmentation check with the help of a clinic expert. Beside such structures, the precise approach should be applied to the ROI and areas of special interest. Even in this case, the segmentation can start from the masks obtained using the fast approach.

The precise segmentation is the most time consuming phase of the entire process; accordingly, the available time resources that were indicated in Step 2 of the procedure should be taken under consideration in order to establish checkpoints and milestones that need to be reached in a predetermined time to better organize the work.

Step 5 - Integration of segmentation
Once that all the basic masks have been prepared, they can be reunited in a single mask describing the shape of the blood pool of the structures to be printed. This operation is performed using Boolean Operations.

The creation of a single mask can be occasionally postponed if the case requires the application of different smoothing and repairing operations to different anatomical structures not only in the segmentation stage, but also during the final modeling. For this reason, independent masks of the anatomical structures should always be preserved.

Step 6 - Final Segmentation Check

During the final segmentation check, the masks produced are cross-examined with the help of a radiologist or a cardiovascular doctor. Clinical indications drafted during the Step 2 are compared with the final results obtained.

Small corrections can be made manually directly during the review process. Heavier modifications can lead to the iteration of the segmentation process that would be guided by a new set of clinical indications, as depicted in Fig. 1.

Step 7 - Part Modeling

Once that the segmentation is finished, the parts need to be prepared for the printing process. Accordingly, some operations must be performed to transform the final segmentation mask, describing the internal volume of the heart, into a printable object.

The segmentation mask needs to be converted to a 3D model and later processed to amend possible mistakes and regularize its surface to improve its manufacturability. If the user has decided to keep some anatomical structures separate in order to apply different modeling steps, the procedure should be applied for each of them.

The resulting mask from the segmentation is first converted into a 3D object, which Materialise Mimics calls “Objects”, thanks to the “Calculate Part” function, which maps the contours of the mask creating a triangulated surface (STL model); “Optimal” settings (Fig. 9a) should be used in the Calculate part function to create the model. Once that a part is created, Materialise Mimics® offers a new set of tools to process the newly created model. Among these, the most useful are the Smooth function and the Wrap function. Such functions are typical functions that can be found in 3D modeling software packages to edit mesh objects (i.e. triangulated surfaces). Accordingly, they can be found in several general purpose environment (e.g. Autodesk Meshmixer, Solidworks). A valid alternative to perform the wrap function is also offered by Geomagic Design X, another 3D modeling software. Online Both perform operations that can be exploited to improve the quality of the generated model. The smooth function removes superficial asperities of the model by repositioning the vertices composing the mesh. The result is a smoother surface. Wrap is applied to close small holes on the surface and to remove tunnels and internal surfaces of the model. The function works by wrapping a new surface around the existing 3D part; such surface is controlled by two dimensions (Fig. 9b): the smallest detail to preserve and the gap closing distance. Increasing the first results in
Fig. 9. (a) Calculate Part tool GUI within Materialise Mimics®; (b) Wrap GUI within Materialise Mimics®.

Table 3

| Smooth – Number of iterations | 5 |
|-------------------------------|---|
| Smoothing Factor              | 1 (fast masks); 0.6 (precise masks) |
| Wrap – Smallest Detail        | 1 mm (fast masks); 0.5 mm (precise masks) |
| Wrap – Gap Closing Distance   | 1 mm (fast masks); 1 mm (precise masks) |

a less-detailed surface, while the second controls the size of the holes that the reconstructed surface will be able to “bridge”, erasing them. The option “protect thin walls” offered in the wrap tool should be generally deactivated, as it causes a dilation of the entire model and should be applied only for masks characterized by small thicknesses.

This procedure proposes the application of a first smooth pass, followed by a wrapping operation. Suggested parameters, applicable for fast or precise masks, are reported in Table 3. Whenever a single mask is created in the segmentation process, the precise parameters should be used for smoothing and wrapping.

Step 8 - Design for Additive Manufacturing

Once the model is finished, it still needs to be processed to improve its manufacturability. Some modifications can be made, in order to reduce the probability of problems during the FFF process and to reduce the fabrication time. This is, as previously discussed, a fundamental element to enable a wider application of 3D printed cardiac models. The procedure considers the use of an FFF printer because its generally the best suited to obtain a rigid model in a short period of time. Other kinds of additive technologies can be used to implement the same step; depending on the technologies, different manufacturing constraints should be considered. FFF build volumes are generally compatible with cardiac models: most common sizes present a work area of 200 mm x 200 mm x 200 mm with lower volumes representing a small portion of the market. Selective Laser Sintering – SLS machines guarantee more freedom for the type of shapes that can be produced, as they do not require support structures, but the production of a part imposes higher costs and higher fabrication times (the build volume needs to be heated, production is optimized when the whole build volume is filled with parts, raw material is more expensive). Moreover, SLS machines are even more expensive and, accordingly, less common. Other plastic additive manufacturing technologies are even more rare/expensive (e.g. Polyjet, SLA) and present similar advantages/drawbacks compared with SLS. FFF Print preparation aims at three goals:

- Generation of a wide and stable base for the print
- Minimization of supports
- Minimization of the volume of the printed part

The first task to achieve is the generation of a wide and stable printing base. This is the most important element, as it goes in parallel with the definition of the printing direction of the model.
The build direction, in turn, influences the amount of required supports, the quality of the surfaces, and ultimately the printing time.

The most favorable position results to be the one depicted in Fig. 10, with the atrium and the ventricle disposed one on top of the other, aligned with the Z-axis of the FFF printer. This produces a model with an even surface quality and minimizes the amount of supports that are required. Moreover, since LVA/RVA surgical operations are specifically interested to the study of the ventricle area, this disposition reduces the supports that need to be attached to the ventricle surface and, ultimately, improves the quality of that area of the printed part.

In order to build a valid base, a planar cut to remove the bottom part of the atrium is performed. This can be done using the “Cut with plane” function, which works on the Mimics Objects. The user needs to select three points defining a cutting plane that is close to perpendicular to axis of the MV (colored in cyan in the figure). Fig. 10 presents an indication for the choice of the cutting plane.

The function splits the original model in two parts, isolating the region to be printed (in red in Fig. 10). The plane can be positioned ad different height, depending on the importance of preserving the atrium shape for the specific clinical case considered, the amount of material that can be removed to save printing time and the size of the planar area required. With this respect, the area should be controlled depending on the total height of the cardiac model: higher models require a wider base to assure stability. The user can also decide to avoid the introduction of a cutting plane whenever the upper part of the atrium is sufficiently planar and can be used with the introduction of a little supports volume to sustain the print.

Minimization of supports can be obtained by removing overhang surfaces (i.e. part of the model that, with respect to the building direction, extend laterally) that are not essential for the final cardiac model. The user can identify such areas according to the clinical indications that were provided in the step 2 of the procedure or during the final segmentation check. They can be efficiently removed with the “Cut with curve” tool, which allows the user to draw a cutting curve directly on the surface of the object. Moreover, support minimization can be tackled even in the subsequent phase, working with the process parameters.

Finally, the minimization of the volume, which improves the building time of the cardiac model, can be tackled by removing parts of the model as previously discussed. This solution is evidently obvious; moreover, unnecessary parts should have already been removed in the segmentation process. However, time resources could have been badly spent or poorly estimated. This phase at the end of the process offer a second occasion to remove additional volumes.

Another approach that can be implemented to minimize the printing volume is the generation of internal cavities. Depending on the shape of the 3D model, this can result in a lower printing time. This can be done by preparing an additional mask representing the cavity to be generated. This “negative” mask is converted to an object using the same process and later used as object to subtract in a Boolean function. At least 3 mm of thickness should be guaranteed across the entire model.
When internal cavities are generated, the user should prepare both the hollow model and the full one in order to evaluate the advantages obtained simulating the printing process in the subsequent step. The time savings obtained with this operation can be minimal and should be indeed controlled; cavity creation can lead to the generation of more support structures and can increase the external surface of the object: both factors negatively affect the FFF production rate.

Step 9 - Print preparation

The model needs to be exported from Materialise Mimics® to be imported into the FFF process software. Every 3D printing software requires an STL file as input to be processed. Accordingly, the model needs to be exported in this format from Materialise Mimics®. This is done by right-clicking on the final model in the object list and selecting “Export STL”.

The file is locally saved and can be imported into the FFF software to prepare the fabrication. The choice of the software depends on the available machine: some systems impose the use of a proprietary software, while less-expensive machines usually rely on non-specific software like Cura [4] or Simplify3D [5]. The specific software used for the execution of the procedure has no impact on the final result.

Table 4 reports a list of FFF process parameters that are valid for every machine; such parameters define the solidity and the superficial quality of the produced model. Additional parameters that could have an impact on the speed of the process (e.g. printing speed) should be determined according to the characteristics of the specific machine.

The use of soluble support material (in case the available system allows it) may improve the end result but usually, considering the application scenario, it is best to avoid the long dissolution process required to remove the supports. Accordingly, breakaway supports are recommended.

Once that the print setup is finished, the user can simulate the printing process, visualizing the resulting cardiac model and support structures as showed in Fig. 11. In this phase, the user should evaluate how much support structures are necessary and where are positioned. If an alternative configuration is identified, the user can reposition the model or even building a new, improved, base. In this case, the user needs to repeat the step 8 of the procedure.

Step 10 – Fabrication

| Parameter            | Value    |
|----------------------|----------|
| Layer height         | 0.2mm    |
| Infill               | 12%      |
| Overhang angle       | 60°      |
| Extruder diameter    | 0.4 mm   |

Fig. 11. Simulation of the printing process. The cardiac model is depicted in green. Support structures are colored in orange.
Fabrication can be carried out using any type of FFF printer. ABS or PLA materials can be used: no specific mechanical properties are expected from this kind of models. Optical properties of the model are often undervalued: white opaque plastic presents the best characteristics to allow a good appreciation of the details. Fabrication times are usually high and can be estimated in at least 10 h of printing for a model composed of LV and LA chambers. Slight changes can be obtained tuning the process parameters (e.g. print speed) but the main factors influencing fabrication times remain the size of the model and its shape.

Method validation

The case taken under consideration [6] for the application of the described procedure is a 59-year-old female admitted to the emergency department for heart failure (HF), with dyspnea started 10 days before. She was formal smoker, affected by hypercholesterolemia and hypertension, on ACE inhibitor treatment at time of presentation. An anterior, evolved MI infarction was revealed by ECG, and 2D-echocardiogram showed a wide apical LVA (6 × 5.5 cm) without thrombus and mild mitral regurgitation. Cardiac MRI confirmed an apical LVA without thrombus, and a transmural delayed enhancement in the myocardium wall. Since the 3D volumetric sequences were not planned in MRI protocol, to optimize surgical planning, based on cardiac CT scan, we decided to generate a 3D print model of the LVA for a better prediction of the residual surgical LV volumes and the shape of the LV and the LVA specifically.

The procedure was applied on this single case but was repeated four times: both for systolic and diastolic phases and both pre and post intervention. Of the four digital models created applying the procedure, two models were printed and provided to the clinicians. The procedure was carried out practically identical both for the pre-operation models and for the post-operation ones. The only main difference being the time resources available for the two cases, with only 48 h (as later described) available to produce the preoperative model. Accordingly, only the process that brought to the generation of the first model will be presented.

A dedicated contrast-enhanced computed tomography (CT) scan (high pitch, dual source) was made according to the following protocol: retrospective ECG-gated spiral acquisition, with tube modulation. Thin slice height (0.4 mm) was used. The data was judged as perfect for the application: specifically, the contrast enhancement obtained in the LA and LV chambers was high.
Fig. 13. Fast segmentation masks; purple – LA and AO; cyan – LV.

Fig. 14. Digital model obtained at the end of Step 7 of the proposed procedure.

The initial segmentation performed with the clinical team highlighted the following points:

- Principal ROI of interest: LVA area (atypical LV shape)
- Secondary ROI: mitral valve area and papillary muscles, as the reshaping of the ventricle could affect the functionality of the valve due to the change in position and function of the papillary muscles.
- Regions that should be represented in the physical model: LV, AV. Main veins and arteries
- Relative interest for the LA
- Limited time: 48 h to produce a rigid 3D printed model
- Landmarks positioned to delimit the boundaries of the aneurysm (principal ROI) – See Fig. 12

Filters were applied as described in the procedure for the generation of data used for the fast segmentation. No border augmentation technique was used in this case. A curvature flow filter was applied to the data for fast segmentation. Table 1 parameters were used.

Fast segmentation was applied to the segmentation of the LA blood pool and to provide a first, rough, segmentation mask of the LV. The precise approach was used to segment the ROI. The process was applied as described in the procedure. The automatic segmentation “heart tool” was tested but its results were judged not acceptable for this application. It is important to note that the high level
Fig. 15. Digital reconstructions performed on the systolic and diastolic phases, pre and post operation.

Fig. 16. Final printed model of the LV/LA chambers.
of the contrast enhancement observed in the CT data has greatly eased the outcome of the procedure. Fig. 13 provides some details on the masks obtained during the process.

The final result obtained at the end of the segmentation and modeling phase, once that fast and precise segmentation masks were assembled is depicted in Fig. 14. As it can be seen from the image, main vessels were almost entirely removed (with the exception of the AO) as their presence was not considered useful by the clinicians. The entire modeling phase required more or less 6 h to be completed. Similar results were obtained on all four models (systolic and diastolic phases, both pre and post operation) that were created for this patient. An additional digital elaboration of the four models was applied to isolate the regions of the aneurysm (red) and of the patch used during the operation to reshape the left ventricular cavity (blue) from the LV blood pool, resulting in the Fig. 15. These were specific requirements that were asked for the specific case study.

The model was printed using 0.1 mm layers using a Makerbot Replicator + printer. PLA white plastic was the selected material. A higher layer value was considered but in this specific case the printing process was to be held overnight; accordingly, no time saving was to be obtained in selecting a lower vertical resolution as the model would have been collected the following morning in any case. The result is visible in Fig. 16.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

No data was used for the research described in the article.

Acknowledgments

[OPTIONAL. This is where you can acknowledge colleagues who have helped you that are not listed as co-authors, and funding. MethodsX is a community effort, by researchers for researchers. We highly appreciate the work not only of authors submitting, but also of the reviewers who provide valuable input to each submission. We therefore publish a standard "thank you" note in each of the articles to acknowledge the efforts made by the respective reviewers.]

References

[1] J.M. Otton, N.S. Birbara, T. Hussain, G. Greil, T.A. Foley, N. Pathar, 3D printing from cardiovascular CT: a practical guide and review, Cardiovasc. Diagn. Ther. 7 (5) (2017) 507–526. OctPMID: 29255693; PMCID: PMC5716949, doi:10.21037/cdt.2017.01.12.

[2] A. Virzì, C.O. Muller, J.B. Marret, E. Mille, L. Berteloot, D. Grévent, N. Boddaert, P. Gori, S. Sarnacki, I. Bloch, Comprehensive review of 3d segmentation software tools for MRI Usable for pelvic surgery planning, J. Digit. Imaging 33 (1) (2020) 99–110. FebPMID: 31236743; PMCID: PMC7064712, doi:10.1007/s10278-019-00239-7.

[3] L. Puggelli, F. Uccheddu, Y. Volpe, R. Furfari, D. Di Feo, Accuracy assessment of CT-based 3D bone surface reconstruction, Lect. Notes Mech. Eng. (2019) 487–496.

[4] Ultimaker cura software - https://ultimaker.com/it/software/ultimaker-cura - last accessed: 17/08/22.

[5] Simplify3D - professional 3D printing software - https://www.simplify3d.com/ - last accessed: 17/08/22.

[6] N. Carrabba, F. Buonamici, R. Furfari, M. Carfagni, M. Vannini, R. Valenti, A.G. Cerillo, N. Marchionni, P. Stefano, Case report: three-dimensional printing model for surgical planning of Left Ventricular Aneurysm: evolution toward tailoring surgery, Front. Cardiovasc. Med. 9 (2022) 852682. Mar. 25PMID: 35402549; PMCID: PMC8990127, doi:10.3389/fcvm.2022.852682.