ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

Three-dimensional Reconstruction of Anatomical Structures: Interactive Software Providing Patient Specific Solutions

Üç-Boyutlu Anatomik Yapı Modellemesi: Hastaya Özgü Çözümleme İçin İnteraktif Bir Yazılım Uygulaması

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ABSTRACT Objective: Recent advances in patient specific three-dimensional (3D) modeling serve as the initial platform for developing computational simulations and tools for prognostic foresight. In this study, we introduce the preliminary results of a semi-automatic software program, TT3D-BMMP (TanTuna 3D-Başkent Measuring and Modeling Program), developed in our laboratory that generates 3D reconstruction from a set of tomographic medical images. **Material and Methods:** The software uses two-dimensional patient dataset, segments the selected anatomical structure then generates surface mesh structure in a universal format of "msh". Segmentation is performed by an automatic algorithm with manual correction option. Post-processing options such as rendering and visualizations may be performed in any programs with post-processor option. In the construction of programming algorithms anonymized computer tomography datasets were used which were obtained from freely available websites. **Results:** The preliminary results of the software were discussed on various anatomical models by means of automatic and manual segmentations, different resolutions, manual corrections, capabilities and limitations. This study offers and describes interactively ever developing, freely available application for 3D visualization of anatomical structures from actual patient cases. **Conclusion:** We believe the software will serve as one of the main platforms for the future studies ranging from patient specific simulations to bio-printing.

Keywords: Image reconstruction; three-dimensional image; patient-specific computational modeling

ÖZET Amaç: Günümüz bilgisayar teknolojileri ardışık tomografik görüntüleri kullanarak anatomik yapıların 3-boyutlu (3B) görüntülenmesini mümkün kılmıştır. Hastaya ait anatomik yapıların 3B görsellerinin, fizyolojik süreçlerin matematiksel çözümlemelerine basamak oluşturması açısından önemlidir. Bu açıdan 3B modellemeler bazı hastalıkların seyri ile ilgili ölçütlerin tahmin edilmesi, tedavilerin hastaya özgü olarak planlaması ve risk değerlendirmesinde önemli bir araç olarak kabul görmektedir. Bu çalışmada, bu alandaki bilimsel bilgi birikimine katkı sağlayabilmek amacıyla laboratuarımızda geliştirdiğimiz bir yazılım, TT3D-BMMP (TanTuna 3D - Başkent Measuring and Modeling Program), uygulaması tartışılmıştır. **Gereç ve Yöntemler:** Yazılım sırasıyla, tomografik kesit görüntülerinden anatomik yapıların sınırlarının belirlenmesi (segmentation), verilerin 3B kartezyen koordinat sistemine yerleştirilmesi ve 3B görselleştirmeye uygun yüzey ağ-yapısının (surface mesh) oluşturulmasını içermektedir. Delphi programlama dili ile geliştirilen yazılım uygulaması, hedeflenen anatomik yapının sınırlarını otomatik olarak ve gerektiğinde el ile çizme/düzeltme yöntemiyle tanımlamaktadır. Otomatik nesne tanıma (feature extraction) prosedürü "radyal map" algoritmasını kullanmakta olup yüzey ağ-yapısı popüler dosya formatlarında saklanmaktadır. **Bulgular:** Düşük düzeyde kullanıcı etkileşimi gerektiren bu 3B organ rekonstrüksiyon yazılımı, açık kaynak web sayfalarından alınan anonim hasta görüntüleri üzerinde geliştirilmiştir. Bazı model çıktıları 3B yazıcı teknolojisi ile üretilerek test edilmiştir. Üretilen solid modeller tomografik kesit görüntüleri ile şekil ve ölçek karşılaştırmaları yapılarak değerlendirilmiştir. **Sonuç:** Bu yazılımın, hastaya özgü anatomik modelleri temel alarak, fizyopatolojik parametrelerin hesaplamalı çözümlemelerinin yapılabilmesi için multidisipliner çalışma olasılıklarının önünü açacağına inanmaktayız.

Anahtar Kelimeler: Görüntü rekonstrüksiyonu; üç-boyutlu görüntü; hastaya özgü bilgisayarlı modelleme

Recent developments in medical imaging technologies provided useful tools for better assessment and understanding of organ function in health and disease. Much of the work in the field has been focused on anatomical and/or structural analysis of body parts for educational purposes at the beginning but increasing number of studies with recently developed tools are directed to clinical applications.[1,2] Historically, the first step of methodological advancement was two-dimensional (2D) image analysis in 1980s. The analysis of three-dimensional (3D) images replaced the key goal as mathematical-model-driven approaches became computationally feasible in 1990s. Recently, advanced imaging and computing technologies are facilitating the work in image-guided procedures with more realistic visualizations.

It is noted that driving data about physiological functions using analytical methods on the image based models represents an area of equal or even greater importance.[2] Application of sophisticated computational methods for image processing and visualization allows examination of 3D reconstructed anatomical structures.[2,3] Production of solid/flexible samples of these virtual anatomical models further enables additive manufacturing (3D printing) for a variety of purposes like medical training or surgical pre-practices.

New technological developments resulted in broader usage of innovative teaching methods such as using computer-aided 3D visualization and 3D solid model printing as supplementary to the classical teaching methods in medicine. It is suggested that computer based 3D applications including 3D games increase the mental rotation ability of medical students and such applications also enhance their understanding of complex anatomical structures together with the mental representation of spatial relationships of different structures.[4] Radiology also plays a critical role in helping medical students to recognize gross anatomical structures and their relationships.[1] One of the most essential aspects of using radiological resources is that it may lead students to realize the dramatic degrees of variations between the patients increasing the accuracy of diagnosis/treatment in their professional medical practice.[1]

Besides medical education, computer-aided 3D visualization and solid model production is also becoming an attractive tool in some clinical cases as mentioned above. It is suggested that these innovative tools may facilitate preoperative identification of structural abnormalities in individual cases with complex structures like extensive angulations. It may also help senior surgeons to manage and improve patient specific surgical/interventional skills of their younger colleagues.[5]

Generation of 3D anatomical models from actual patient data brings new practices entitled as "patient specific simulation" to the agenda. Another successful application of these models is the estimation of risk factors for vascular pathologies by monitoring spatial and temporal patterns leading to changes in hemodynamic forces.[6-8] The well-known engineering method of computational fluid dynamics (CFD) also takes place in medical simulations which helps to calculate hemodynamic parameters for every volume element defined in 3D realistic vessel models, recently. Patient specific simulation will be the core of "clinical diagnostic expert systems" as it provides an important tool for the management of patient specific treatment also assessing the risk of complications.[6,8]

Methods for 3D reconstruction of anatomical structures are of special interest for a variety of perspectives as briefly outlined above. In other words, virtual model generation is the starting point of any project and is achieved by the software specially developed for this purpose. There are several 3D reconstruction software programs currently available. Some of them are specialized to very specific area of interest while the others are developed for more general use.[5,9] These programs usually require advanced knowledge of computer literacy and familiarity for the end-user. In the present study, we introduce the preliminary results of a semi-automatic software program developed in our laboratory that generates 3D organ reconstruction from a set of tomographic medical images. The software serves as the main platform for the future studies ranging from teaching to patient specific simulations. This user-friendly software has both manual and automatic segmentation options aiming to increase accuracy when needed.

MATERIAL AND METHODS

The software program, "TT3D-BMMP" (TanTuna 3D - Başkent Measuring and Modeling Program), presented in this study has been developed for generating 3D virtual models of the selected anatomical structures in the body. This study was conducted in accordance with the Helsinki Declaration. The study was approved by Başkent University Institutional Review Board (Project no: DA16/44) and supported by Başkent University Research Fund. Local ethics committee approval was not necessary for the study since the anonymized computer tomography (CT) datasets obtained from the Dicom Library and Osirix websites (https://www.dicomlibrary.com/, https://www.dicom-library.com/) were used in constructing programming algorithms (datasets at Osirix websites were freely available at the time of writing).

GENERAL DESCRIPTION OF THE SOFTWARE

The software program was written in Borland Delphi version 6.0 programming language for Microsoft Windows 98 (Microsoft Corporation, Seattle, WA) and higher operating systems running independently, free from any other commercial platform. Image editing procedures use zoom and shift functions of "ALZoomImage", a flicker-free image Delphi component (www.stella_209.extra.hu; website is no longer available).

Operational screen design, variables and options were simply organized so that the graphical user interface provides users with a friendly environment. A sample screenshot of a typical graphical user interface is given in Figure 1F. The figure includes a set of segmentations performed on 6 sequential images (Figure 1A-F) taken from different levels of a CT dataset. Right after loading the data set all images were calibrated before starting segmentations.

PRE-PROCESSING

A set of images of 2D tomographic slices in Digital Imaging and Communications in Medicine (DICOM) format (taken by CT or MRI) is imported into the program in binary JPEG format then the selected anatomical structure in each loaded CT slice is segmented using a special image analysis algorithm. When the segmentations were completed, the 3D surface modeling of the selected anatomical structure was constructed and saved for further processing. In this step, the solid anatomical structure was discretized into equivalent system of many smaller units (finite elements) and interconnected in an order at points common to two or more elements and/or boundary lines and/or surfaces. The product of this process was ready for either 3D visualization in the computer screen or further physiological computation. Further computations, out of scope of this study, may include finite element analysis that is a numerical method for solving temporal and spatial problems of physics and engineering where analytical solutions cannot be obtained.
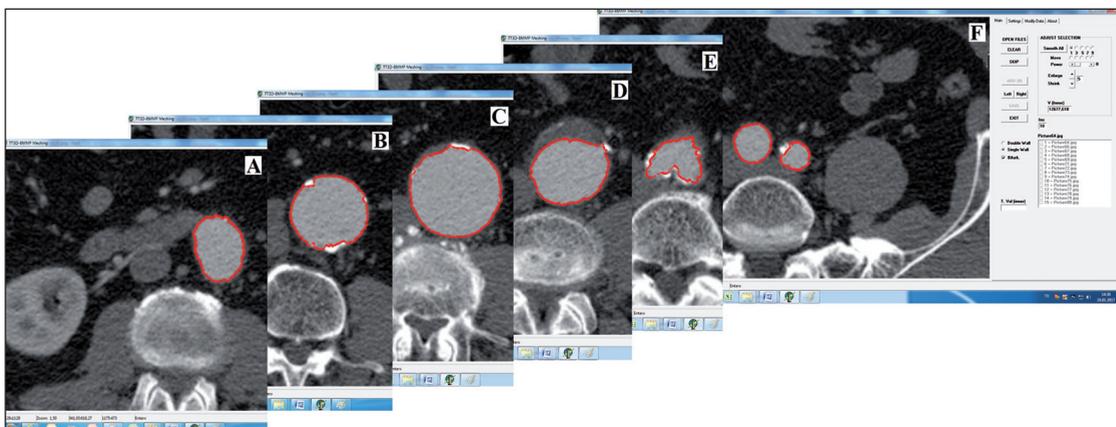
FIGURE 1: Serial screenshots taken from segmented abdominal aorta in the images of successive CT-scans (A-F). Graphical user interface of the software is shown in (F).

The discretization process includes segmentation and surface mesh generation steps.

SEGMENTATION

Defining the Cartesian coordinates of the contour of an anatomical structure of interest in a 2D image is performed by a specific feature extraction method. The image of body scan may show wide range of color and structural heterogeneity, therefore in TT3D-BMMP we also added manual segmentation option where in the case of automatic definition of the coordinates is not successful enough. In the automatic method the "radial map" algorithm was used. The drawings given in Figure 2 depict the algorithm, schematically. The algorithm scans pixels of the image starting from the center of selected circular structure to distal in radial direction until the matching condition is satisfied at a given threshold value. The iteration of this scanning algorithm starts at 12 o'clock position and continues in clockwise (arrow) direction in predefined angular precision. The accuracy and precision of the discretization are defined by the related variables of radial map algorithm. The schematic presentation of samples given in Figure 2A-D emphasizes on the segmentation differences in the case of four different angular precisions obtained using four different radial angles (α). Manual segmentation on the other hand discretizes structures with complex geometry by drawing the computer mouse on its border. Since the number of sampled points on the border is defined by the radial angle, it should be applied to all images in the tomographic dataset. The same angle is also valid for manual segmentation otherwise surface mesh construction error is un-avoidable. Either method, namely automatic

and manual, ask for user's confirmation to accept the segmentation and when needed let manual adjustment (correction) on the segmented data such as smoothing and reshaping. The corrections definitely cause an increase in processing time yet guarantee having the accurate results.

MESH GENERATION

Segmented data from all the images in the tomographic dataset are placed on the same 3D coordinate system. The common points that constitute the 3D solid geometrical structure are interconnected so that two (lines) and three points (face) elements are created by the software, automatically. The 3D surface mesh model of the selected anatomic structure created in this way is then saved in a file format of ".msh" which may be imported into the popular software programs for post-processing. A sample of schematic surface mesh generation employed by TT3D-BMMP was visualized in a post-processor and presented in Figure 3.

POST-PROCESSING

Post-processor software programs contain general purpose sophisticated programming routines such as sorting, printing and plotting 3D models and selected results from further computation in the processing phase. Therefore, developing the post-processing module was intentionally left out of scope of our software (TT3D-BMMP) instead Gmsh©, free 3D finite element mesh generator with built-in pre- and post-processing facilities, was used under General Public License (GPL) for visualizing our 3D virtual models.[10] Gmsh also permits exporting ".msh" files into
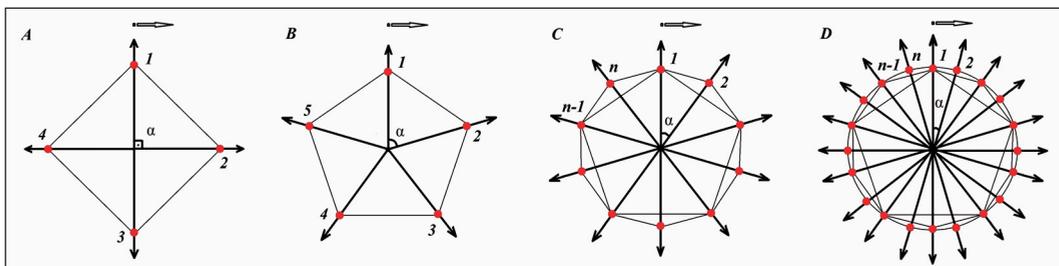
FIGURE 2: Schematic presentation of segmentation using radial mapping method. Segmenting the same circular object using different radial angles (α) were resulted in different number of points (red) starting from position marked as "1" to "n" in clockwise direction **(A-D)**. The higher number of points **(D)** the higher precision yet increased processing time.
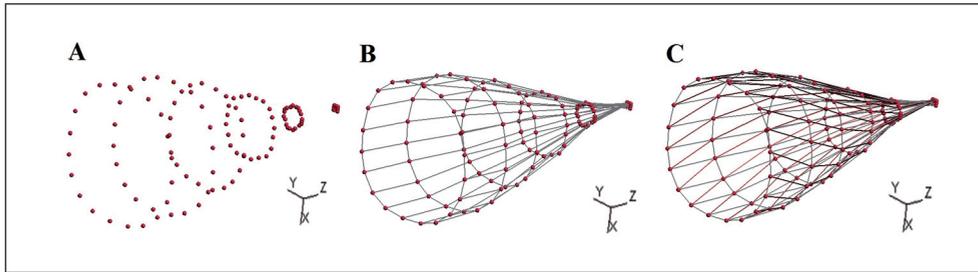
FIGURE 3: Schematic presentation of surface meshing. The points defined at each slices for an object are interconnected in a way that they reconstruct the 3D mesh structure of the object. The points of defined for each slice placed in a Cartesian coordinate system **(A)**. Reconstructed surface mesh structure of the object with rectangular **(B)** and triangular **(C)** polygons.

printable stereolithography (.stl) file format so that a physical model of the virtual model may be produced using a 3D printer.

RESULTS

Sample applications of segmentation for a thrombotic aorta images were presented in Figure 4A-C. The presented segmentation is produced automatically by clicking the lumen of aorta and no further correction like smoothening was used. As described in the previous section decreasing the radial angle (α) improves the resolution of segmentation. This rule was demonstrated in Figure 4A through Figure 4C.

Figure 5A demonstrates a successful application of automatic segmentation on a relatively irregular anatomic structure. In Figure 5B, on the other hand, an improper automatic segmentation for an irregular structure is given. Besides automatic segmentation, the software also provides a tool to draw the outlines of a structure of interest, manually (Figure 5C,D). Manual drawing on such an irregular structure is presented in Figure 5C. Once the structure becomes more irregular in outline; manual drawing rather than automatic segmentation better be preferred. Once the drawing is checked and corrected manually as desired the software finalizes the segmentation automatically with the resolution of selected "α" angle (Figure 5D). Another combination of choice might be applying automatic segmentation first followed by manual correction. This may be easier to perform sometimes as user has the chance to see the automatic segmentation of the image and decide what to do. If it seems that automatic segmentation is not satisfactory enough which cannot be easily corrected automati-

cally or manually user can directly switch to manual drawing after clearing the automatic segmentation.

The software also provides tools for double and paired segmentations on the same image (Figure 6A, B). Double segmentation is automatically created when the wall of a tube-like organ is clicked as inner and outer borders marked in different colors (Figure 6A). The vessel wall or more precisely the lumen and the outer border of the aorta are discretized by double segmentation method helps easily tracing the spatial changes in aortic wall. User should keep in mind that luminal border is the actual automatically segmented component as the outer border is calculated by applying the wall thickness so it may be subject to more careful corrections when needed. Paired segmentation as the second option is useful when a tubular structure bifurcates to be reconstructed as a whole. This option can also be used to outline two distinct structures in the same image as well. In paired segmentation two structures can automatically segmented by two clicks when the option is selected (Figure 6B). Both options are also available for manual drawing and manual or automatic corrections at a resolution of selected "α" angle similarly.

Three dimensional models prior to post-processing of the three tissues/organs are presented as the products of TT3D-BMMP, namely kidney, abdominal aorta with aneurism and femur bone in Figure 7A-C. In the figure set; segmented data points of kidney (7A), surface mesh structure of abdominal aorta with aneurism above iliac bifurcation (7B) and surface mesh structures of femur bone (7C) were presented.

Various scenes of the digital kidney model are given in Figure 8A as the output of post-processor
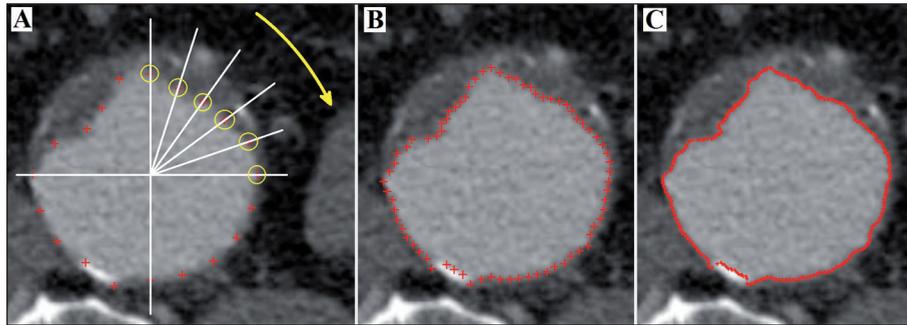
FIGURE 4: Samples of automated segmentation of thrombotic abdominal aorta. **(A)** shows the application of radial mapping method on a circular object, schematically. **(B)** and **(C)** show the resultant segmentations obtained by using different radial angle (α) (red plus sign). Notice the transient increase in precision from **(A)** to **(C)**.
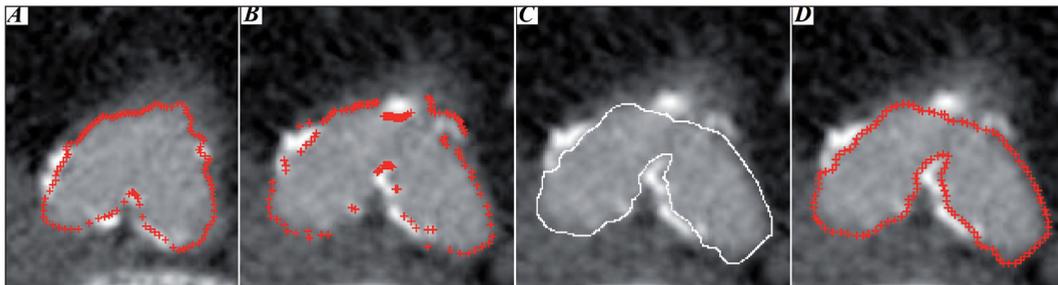
FIGURE 5: Successful application **(A)** of automated segmentation (red plus sign) for an almost circular object and unsuccessful application **(B)** for an irregular object which is the next slice after A. Manual drawing (white line) may be necessary for an irregular object **(C)**. After manual drawing the points are calculated in accordance with the radial angle and placed (red plus sign) on the image **(D)**.
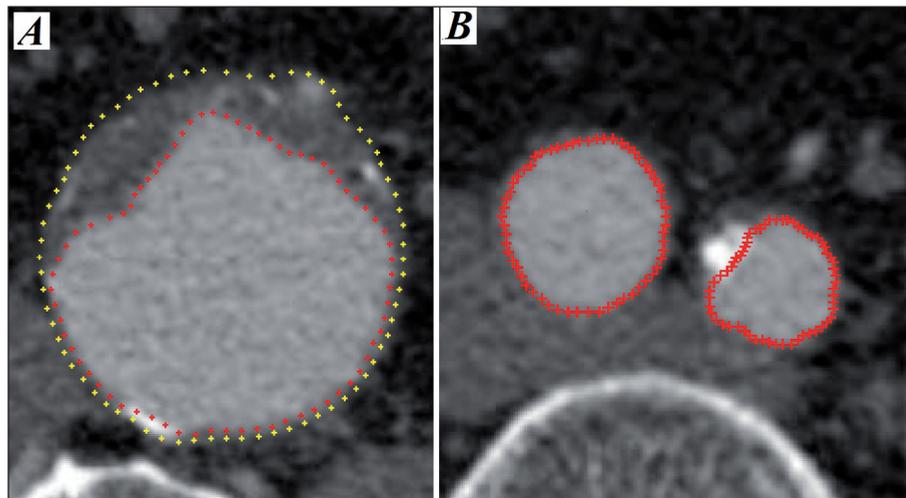
FIGURE 6: The software also has double segmentation **(A)** and paired segmentation **(B)** in an image option. Double segmentation discretizes inner (red plus sign) and outer borders of the object such as blood vessel if applicable. Paired segmentation option is applicable when bifurcation occurs in the following slices as it happens in abdominal aorta or carotid artery.

modality of Gmsh© software. As it is apparent in its mesh presentation of the kidney (Figure 7A), the slice thickness is also an important parameter defining the accuracy of 3D model. Digital (Figure 8B) and phys-ical (Figure 8C) model of abdominal aorta with aneurism is given in various perspectives. Femur bone is given in Figure 8D and Figure 8E as again digital and physical models. Femur bone was recon-

structed in two pieces in order to fit into the printing area of "Raise 3D N2" printer.

DISCUSSION

Technological advances in diagnostic imaging increasingly offer useful information regarding anatomical structures and physiological functions. Dedicated image analysis software specially designed for patient specific anatomical modeling provide detailed quantitative evaluation and facilitate the management of treatment.[8,9] It is believed that today's studies in basic sciences will further lead to the development of sophisticated medical tools of the near future which is called "Clinical Diagnostic Expert Systems".[5,8] Therefore, besides its impact on medical education, the patient specific 3D modeling studies will also serve as the initial platform for computational simulations of physiological parameters and developing tools for prognostic foresight.

Three dimensional modeling tools offered for medical use are either commercially available software or open source freeware programs. The commercial programs have mostly limited functions in highly narrow fields and its implemented algorithms are not open to researchers for further development to be used for specific areas of interest.[9] Open source software on the other hand is usually multifunctional and offers transparency and re-coding options to its users. It addresses to users in wide range of field therefore computer knowledge in professional level is needed. From the technical point of view, another perspective is whether the software is a stand-alone executable application so
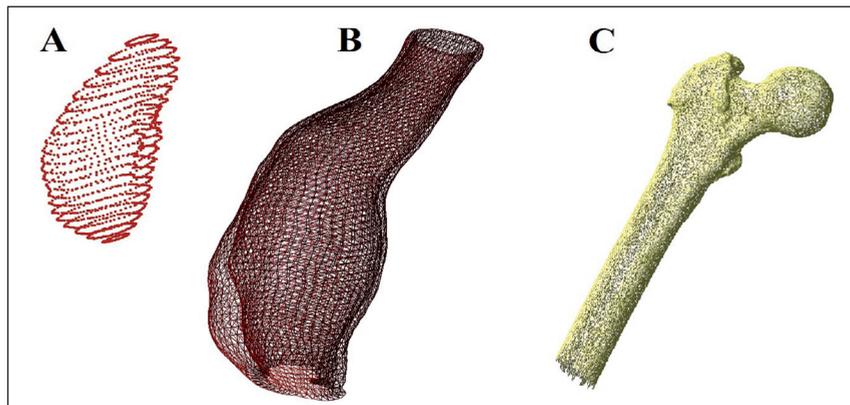
FIGURE 7: The points segmented from a normal kidney placed in the Cartesian coordinate system **(A)**, surface mesh structure of abdominal aorta (B) and upper half of femur bone **(C)**.
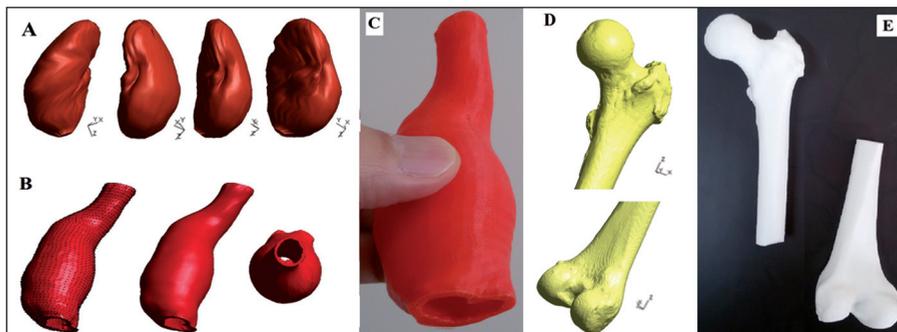
FIGURE 8: Three anatomical structures were reconstructed by TT3D-BMMP software, rendered and visualized by Gmsh post-processor software and printed in Raise 3D N2 printer. The post-processor outputs of kidney, abdominal aorta and the pieces of femur are given in the inset **(A)**, **(B)**, **(D)** and the 3D printer outputs of abdominal aorta and femur are given in the inset **(C)**, **(E)** of the figure.

that the users use it without dealing with technical details or not.

The proposed stand-alone freeware application, TT3D-BMMP, for generating 3D tissue/organ reconstruction from a set of tomographic 2D medical images uses semi-automatic segmentation procedures. Currently, this project has a number of limitations. Although validity and reliability aspects of the software will extensively be discussed in a separate study, we may state that the automatic segmentation with interactive manual correction procedures increases the reliability of reconstructed 3D model as well as reduces the inter- and intra-operator variability.[11] Another limitation of the software for the moment is the time interval needed to be spent to complete 3D reconstruction. This issue is better to be discussed together with the primary aim of user which is in this case not the processing time but rather the accuracy. It is obvious that achieving an accurate image analysis result can only be reached by correction with naked eyes by a professional which is a time consuming process. Additionally, semi-automatic design of a software program guarantees an accurate reconstruction by even less skilled staff providing time and cost effectiveness.[12] Availability of dual application option increases the reliability of the software giving the chance to the end user approve accuracy/time balance. The software also provides calibration bar, adjustment tool for slice thickness, threshold adjustment and precision options, smoothing single segmented (radial plane) and reconstructed mesh data in longitudinal (axial) direction and volume calculation.

The interactive design of the software can provide users mental picture of anatomy and relationships that may lead better understanding than that of 2D atlases.[1] The result of this preliminary study demonstrates the potential impacts of a transfer of 3D modeling techniques into various fields of medicine. Future work would include better generation of more complex 3D models, producing further educational models such as setup for vascular interventional training, creating platform for computational physiology, etc.

CONCLUSION

In summary, this study offers and describes user-friendly software for 3D visualization of anatomical structures from actual patient cases. The software, TT3D-BMMP, is a comprehensive and freely available complete Windows® application for academic purpose. The software can be obtained directly from the corresponding author. The most significant advantage of the presented software is the availability of authors to modify and improve it according to specific needs of the end users comments and/or suggestions. This property will also open a broad window to further develop it to be used for specific clinical perspectives. As we are in information era; digitalization of patient specific data also allows the exchange of ideas worldwide prior to any application on the patient. We believe the software presented in this study will initiate the multidisciplinary studies that may lead scientific contribution into the related fields.

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