Developing Computational Models to Design 3D Printed Scaffolds Using CT Imaging to Reconstruct Actual Bone Defects

K. B. Udayana Piyadeva[1]*, Angelo Karunaratne[1], Udeshi Pramodya Wickramarchchi[2], Sandamini Wanigasooriya[1], R. Gnanasekaram[3], T. P. Miyanawala[1]

[1]Department of Mechanical Engineering, University of Moratuwa, Moratuwa, Sri Lanka

[2]Department of Zoology and Environment Sciences, University of Colombo, Colombo, Sri Lanka

[3]Accident and Orthopaedic Unit, The National Hospital, Colombo, Sri Lanka

Research Article

ABSTRACT

The use of patient-specific scaffolds for the treatment of bone and soft tissue defects formed by accidents and tumour resection is considered an emerging clinical need. We present a method to model bone defects using micro-CT images of bioactive glass scaffolds to generate a reliable computational model that will address the surgical complications caused due to conventional scaffold development methods. The proposed method utilizes two algorithms to develop an automated defect modelling system with high accuracy.

In this article, we discuss the effectiveness of biocompatible materials and bioactive glass scaffolds as bone defect treatment strategies in comparison to the use of fundamental grafting methods and how computational models are being used for bioactive scaffold generation. Our proposed methodology explains the procedure of bone segmentation using CT images, grayscale imaging, image filtering, and feature extraction. We conclude with recommendations for future optimizations of the proposed methodology.

Keywords: 3D printed scaffolds; CT imaging; Bioactive glass; Computational models; Bone defects

INTRODUCTION

Animal locomotion is facilitated by the force of muscles acting on a rigid skeletal system. There are three types of skeletal systems in the animal kingdom: Hydraulic skeletons, exoskeletons, and endoskeletons. The human skeleton is categorized as an endoskeleton which is an internal skeleton composed of hard and mineralized bone tissue that facilitates the movement of vertebrates by its attachment to muscles. The adult human skeleton consists of 206 bones involved in providing support, protecting the body, and serving as levers for forces produced by the contraction of skeletal muscles (Figure 1). Bone is the building material of the human skeleton and it is a special form of connective tissue [1].

Figure 1. The organization of the compact and spongy bone tissue, shown at three levels of detail.
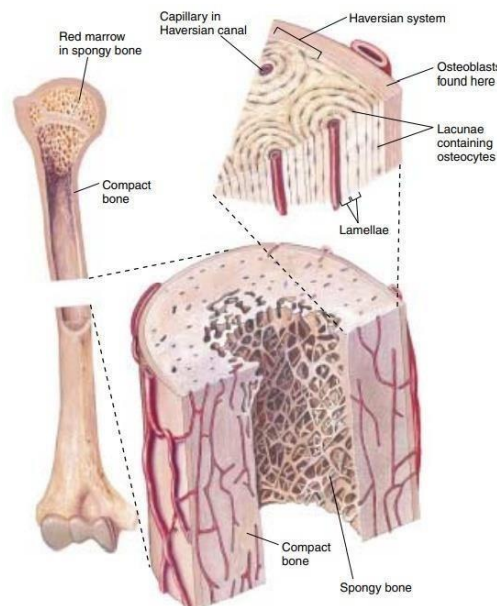
Compact bone consists of a densely packed osteon or Haversian system. The osteon consists of the Haversian canal, which is the central canal surrounded by the concentric rings (lamellas) of the matrix. Between the matrix rings are osteocytes located in the lacunae. The lighter and less dense spongy (cancellous) bone consists of trabeculae which are organized to provide maximum strength.

Bone tissue is reconstructed continuously throughout human life [1,2]. Defects may occur due to various congenital or acquired conditions. Congenital bone anomalies are caused commonly due to the absence of or mal development of bones (such as zygomatic hypoplasia in Treacher Collins syndrome (TCS) or fibula hemimelia) whereas the acquired bone defects are often caused due to trauma, infection, neoplasm, or surgical resection. The global incidence of bone disorders is on the rise and thus, the use of effective potential alternatives for bone replacement has become a timely requirement. The incorporation of foreign bodies such as tissue-engineered scaffolds is a reliable candidate identified to have great potential for therapeutics and supporting tissue formation. It is an emerging alternative to the conventional use of bone grafts that provides an effective replacement for missing bone implants and for areas requiring mechanical strength and structural support.

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Treatments for bone defects

Bone defects are conventionally treated using autografts (tissue from the person's own body), allografts (from a donor of the same species), or xenografts (from a donor of a different species) [2]. However, due to several limitations of natural bone grafts and implants such as disease transfer, limited availability and reproducibility, donor scarcity, alterations in the properties of natural matrices due to sterilization, and immune rejection it is vital to have an alternative material to the bone such as biocompatible materials including bioactive glasses and bioactive glass scaffolds.

Biocompatible materials

Research on synthetic biocompatible polymers for tissue engineering and regenerative medicine applications has been carried out extensively [2-4]. Synthetic bone grafts are produced using metals, ceramics, polymers, and their combinations (hybrid materials and composites) in various morphologies such as cylinders, screws, pins, plates, and rods, as well as formable pastes and gels [2].

Bioactive glasses

Bioactive glasses are currently used as implantable materials for the treatment of various types of bone disorders and diseases [5]. They can stimulate bone regeneration and are more effective compared to other bioactive ceramics. Larry Hench's 45S5 Bioglass® was the first artificial material that was found to form a chemical bond with the bone, launching the field of bioactive ceramics [4]. Several key benefits have been attributed to bioactive glasses related to their application in bone remodelling, including their ability to bind to living tissue and enhance osteoblast growth and proliferation, stimulate osteogenesis and angiogenesis, and local induction of antibacterial and antifungal effects [5-7].

Bioactive glass scaffolds

The first bioactive glass was invented by Larry Hench at the University of Florida in 1969. Professor Hench worked to find a material that could bond to bone, later termed 45S5 and Bioglass®, which bonded with bone so strong that it could not be removed without breaking the bone. This is the beginning of the field of bioactive ceramics with various production using new materials on bioactive glasses.

Bone and soft tissue defects formed due to accidents and the removal of tumours are a major problem that requires treatment with patient-specific scaffolds. Bioactive glass scaffolds can be used to treat such bone defects. The role of these scaffolds is to fill the defect, stimulate new bone tissue growth, and get resorbed over time as they are replaced by newly formed bone. The success of this process depends on the technology available to generate reliable, fully integrated,

complex, three-dimensional, and controlled porous scaffolds of the exact shape and size of the replacement of the bone cavity or defect [4].

Scaffolds made of different biomaterials including bioactive glass are currently in use. However, the production of scaffold involves physiochemical events such as the sintering process which leads to geometrical deviations of the scaffold. During the sintering process, intrinsic events such as densification may result in shrinkage of the whole scaffold. Hence, the geometrical mismatch between the scaffold and the defect may occur contributing to post-surgery complications including cancers. This mismatch can be modelled based on strut level micro-CT analysis and the related algorithms can be used to predict the scaffold to be 3D printed [4-7].

Micro-CT images of bioactive glass scaffolds are used to generate a computational model that will address the geometrical deviations during the sintering process. Meanwhile, 3D-CT bone scans are collected from patients and the images are used to model the defective area of the bone. Finally, the actual scaffolds to be 3D printed will be predicted by applying the generated computational model to the modelled defects.

Computational models for bioactive scaffold generation

3D printing is used to create precise micro scale architectures of bioactive glass scaffolds. But there is no common method or platform for the controlled design and manufacture of 3D-printed constructs for tissue engineering [8]. In addition, there is no specific method to detect and model the bone defect used to create the patient-specific scaffold using bioactive glasses. Therefore, in this study, we aim to develop a computational model to design 3D printed scaffolds using CT imaging for effective reconstruction of actual bone defects.

MATERIALS AND METHODS

The proposed methodology is comprised of several steps including bone segmentation, algorithm selection, grayscale imaging, image filtering, and feature extraction which are reviewed in detail below.

Bone segmentation using CT images

This process extracts the bones from CT images using Visualization Toolkit (VTK) libraries. Figure 2 depicts the two recruited study approaches that utilize the manual and automatic defect detection methods. CT images are usually stored in the format called DICOM (Digital Imaging and Communication in Medicine) with the extension.dcm. Both VTK and MATLAB platforms contain the required functions to read DICOM images. The data type is uint16, which needs to be converted to double for basic operations. Machine learning can be used to train images and to detect the defects from CT scans.

Figure 2. Pipeline of the current approach for virtual bone defect reconstruction. This diagram illustrates two approaches that can be used to construct defects. Both algorithms use NVIDIA AI-assisted segmentation to model the defects.
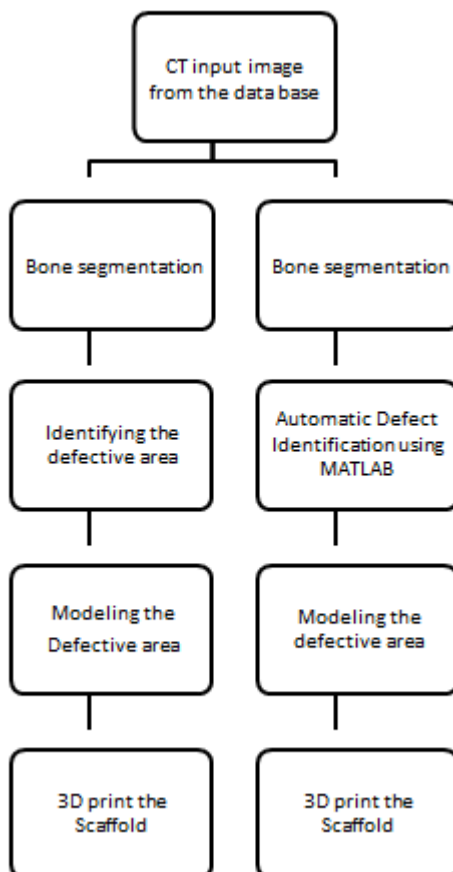
Machine learning

Machine learning teaches computers to learn from data. Computational methods are used by machine learning algorithms to "learn" information directly from data without depending on a predetermined equation as a model. The algorithm adaptively improves its performance as the number of samples available for learning increases [9]. Machine learning algorithms find natural patterns in data that generate insight and help to make better decisions and predictions such as critical decisions in medical diagnostics [10]. With the advent of big data, machine learning has become especially important for solving problems in areas such as; (a) natural language processing, (b) automotive, aerospace, manufacturing, and predictive maintenance, (c) image processing and computer vision, face recognition, motion detection, and object detection, (d) computational biology, tumor detection, drug discovery, and DNA sequencing [11].

How machine learning works

Two types of techniques are being used in machine learning: Supervised learning; which trains a model on known input and output data so that it can predict future outputs, and unsupervised learning; which detects hidden patterns or internal structures in input data [11].

Supervised learning: In supervised learning, evidence-based forecasting models are built in the presence of uncertainty. A supervised learning algorithm takes a known set of input data and a known set of responses corresponding to the input data (output) and trains a model which can generate reasonable predictions in response to new data. This learning uses classification and regression techniques to develop predictive models (Figure 3).

Classification algorithms perform the following discrete predictions–e.g.: whether an email is genuine or spam, or whether a tumor is cancerous or benign. Classification techniques classify input data into categories. Applications of classification include medical imaging, speech recognition, and credit scoring [8-11].

Regression techniques perform the following continuous predictions–e.g.: changes in temperature or fluctuations in power demand. Some of the applications include electricity load forecasting and algorithmic trading [8,9].

Figure 3. Machine learning techniques [9].
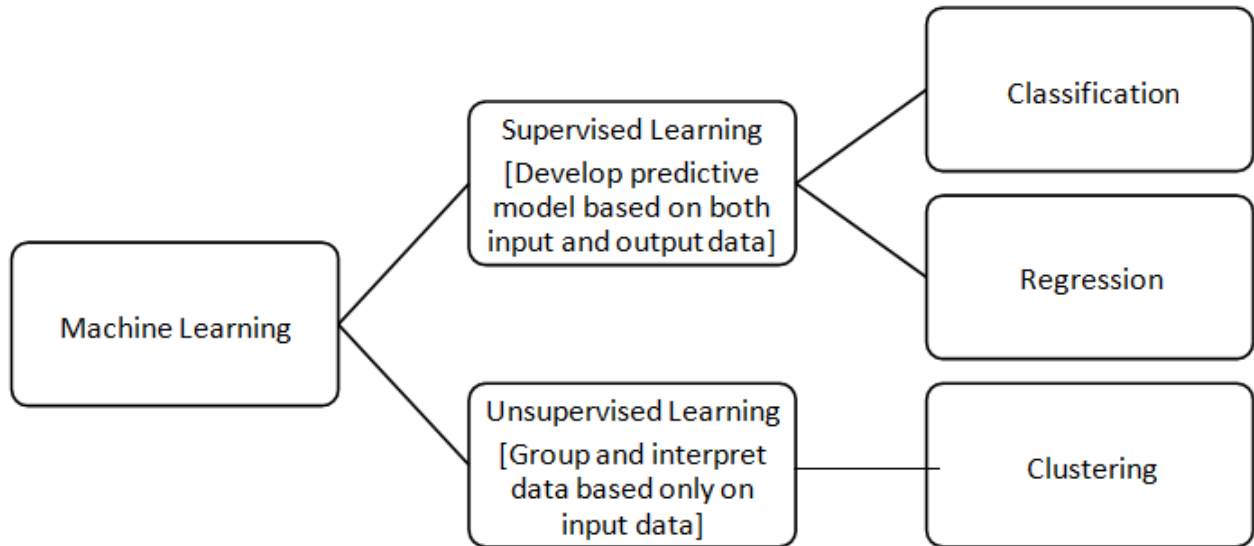
Unsupervised learning: This method identifies hidden patterns or intrinsic structures in data. It is used to detect inferences from datasets consisting of input data without labelled responses. Clustering is the most common unsupervised learning technique [9-11] where similar entities are grouped together. Gene sequence analysis, market research, and object recognition are some of the applications of unsupervised learning. The goal of this unsupervised machine learning technique is to find similarities in data points and cluster similar data points. For the purpose of the current study, the K mean clustering technique, one of the most widely used algorithms has been used (Figure 4).

Figure 4. Clustering patterns in the data. The algorithm finds patterns in data and separates them into multiple subgroups based on their similarity.
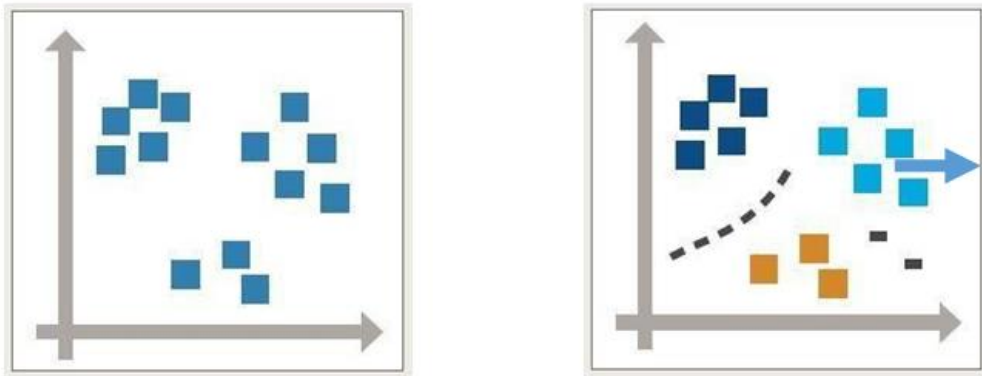
Selecting the appropriate algorithm

Machine learning is a good option since we have a complex task or problem involving a large amount of data and lots of variables, but with no existing formula or equation. There is a wide spectrum of supervised and unsupervised machine learning algorithms, each taking a different learning approach. There is no best method or one size that fits all. Finding the right algorithm is partly just trial and error, where, even highly experienced data scientists are unable to predict whether an algorithm will work, without trying it out [9]. Illustrated below is a summary plan utilized to select the most appropriate algorithm for machine learning (Figures 5 and 6).

Figure 5. The process of selecting an algorithm [9].
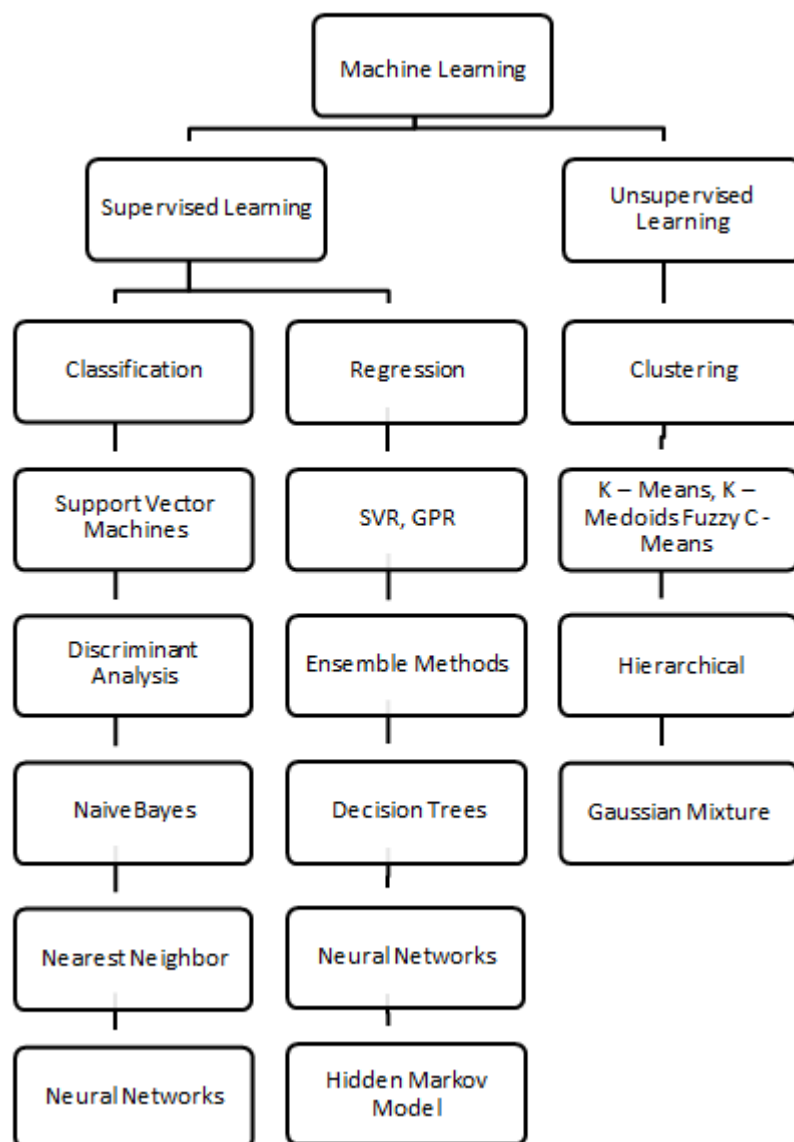
Proposed method

In this project, we present a method to model the bone defects using CT images utilizing two algorithms. As per the literature survey, it is clear that an automated defect modelling system is essential as high accuracy is needed. Automated modelling of bone defects in CT images involves feature extraction and classification using machine learning algorithms. Therefore, the current study involves the following steps as depicted in Figure 2.

Grayscale imaging

Clear output images of detected tumors cannot be obtained since CT images are comprised of RGB. Hence, the input images are initially converted to grayscale where brightness levels of the red (R), green (G) and blue (B) components are each represented as a number from decimal 0 to 255, or as a binary notation from 00000000 to 11111111.

Image filtering

Image filtering is essential as fine details are required. All grayscale images are filtered using imfilter (MATLAB) with the predefined function fspecial, which produces several kinds of predefined filters in the form of correlation kernals. The unsharp masking filter makes the edges and fine details in the image crisper.

Feature extraction using bag of features

Image classification, or object recognition, is the process of identifying a specific object or class of objects in an image or a video. MATLAB Computer Vision System Toolbox consists of a variety of algorithms, tools, and techniques to build image classification and object recognition systems. This approach is used to recognize images using the "bag of Features" technique which is also known as the "bag of words". This technique uses the visual category classification process to define a category label for an image being tested. Categories may contain images that represent any object, for example, dogs, cats, trains, or boats.

The bag-of-words technique was developed to compute the vision from the word of natural language processing. Images do not contain discrete words, therefore it is required to construct a "vocabulary" of visual words by extracting feature descriptors from representative images of each category. Feature extraction is a process of dimensionality reduction that efficiently represents interesting parts of an image as a feature vector. The

Speeded-Up Robust Features (SURF) detector can be used to find the interesting points in images and encode information about the area around the points as a feature vector.

Feature descriptors can also be extracted by defining a regularly spaced grid in addition to the use of the SURF detector. But this grid method may lose fine-grained scale information, so it is recommended only for images that do not contain distinct features, such as an image containing scenery, like the beach. In contrast, a SURF detector would provide a greater scale invariance. However, by default, the algorithm runs the 'grid' method [10].

Figure 6. Extracting visual words from training images. In the feature detection step specific features are extracted (extract keypoints) from each training image.
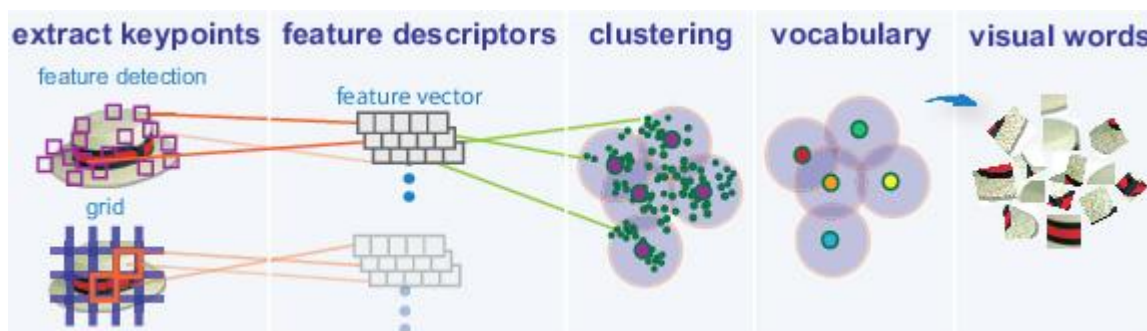

Extracted raw features are stored in matrices as feature vectors (feature descriptors). Interesting parts of an image are represented as a compact feature vector as result of dimensionality reduction in the feature extraction. Then the dataset is portioned into semantically meaningful clusters. Since images do not contain discrete words, it is required to construct a "vocabulary of visual words by extracting feature descriptors from representative images of each category. Extracting the characteristics from all groups of images and developing a visual vocabulary by removing the number of characteristics through quantization of characteristics space using the K-mean clustering method are one of the

approaches where this can be solved using the bag of the features function. K-means clustering partitions the data into k number of mutually exclusive clusters. How well a point fits into a cluster depends on the distance from that point to the center of the cluster. This is best when the number of clusters is known and when the clustering data set of interest is large.

Each category from the encoded images is fed into a classifier training process represented by the 'train Image Category Classifier' function. But this function relies on the multiclass linear SVM classifier from the Statistics Machine Learning Toolbox. The trained classifier can be evaluated by first testing it with the training set, which should produce a near-perfect confusion matrix, that is, with ones on the diagonal. The rest of the images can be evaluated using the classifier on the validation set. By default, the evaluate function returns the confusion matrix, which is a good preliminary indicator of the ways properly the classifier is performing. The trained classifier can be tested by changing different parameters until satisfactory results are obtained. A newly trained classifier can be applied to categorize new images (Figure 7).

Figure 7. The image shows the cluster centers [10].
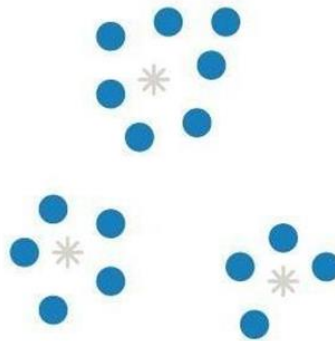
Confusion matrix

This matrix shows the accuracy of the recruited classifier. It represents the correct classification as 'true positives' or 'true negatives', and incorrect classifications as 'false positives' or 'false negatives. This is particularly important in diagnostic tests for the presence or absence of a particular condition or disease based on a single test. The True Positive Ratio (TPR) indicates that the ratio predicted by the modal is positive and true while the False Negative Ratio (FNR) indicates that the ratio predicted by the modal is negative and false [7-11].

RESULTS AND DISCUSSION

MRI bone scan images were segmented using VTK python and the CT DICOM images were segmented and extracted (Figure 8). Bone segmentation algorithm (Appendix A) reads the series of dicom images and extract the bones from bone CT scan images. Volume of the skull area was 745597 mm^3 and area of the defect was 6643 mm^3.
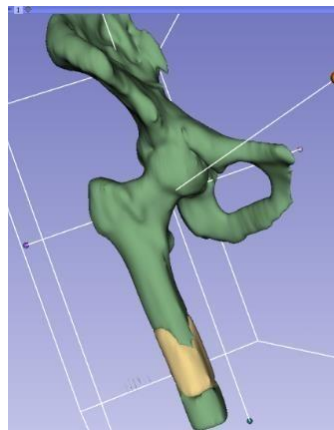
The defective areas reconstructed using the 3D slicer NVIDIA AI-assisted segmentation are depicted in Figures 9 and 10. The result is shown in Figure 11a after boundary points based segmentation. According to the Figures 11a and 11b there is small gap between the actual defect and the generated defect to compensate the defective area. We have to develop our algorithm with a new segmentation that can store the models to train the algorithm [12-14].

Marking the boundary points of the defective area was the first step of the defect reconstruction pipeline. Then AI algorithms construct the model of the defective area [14-16].
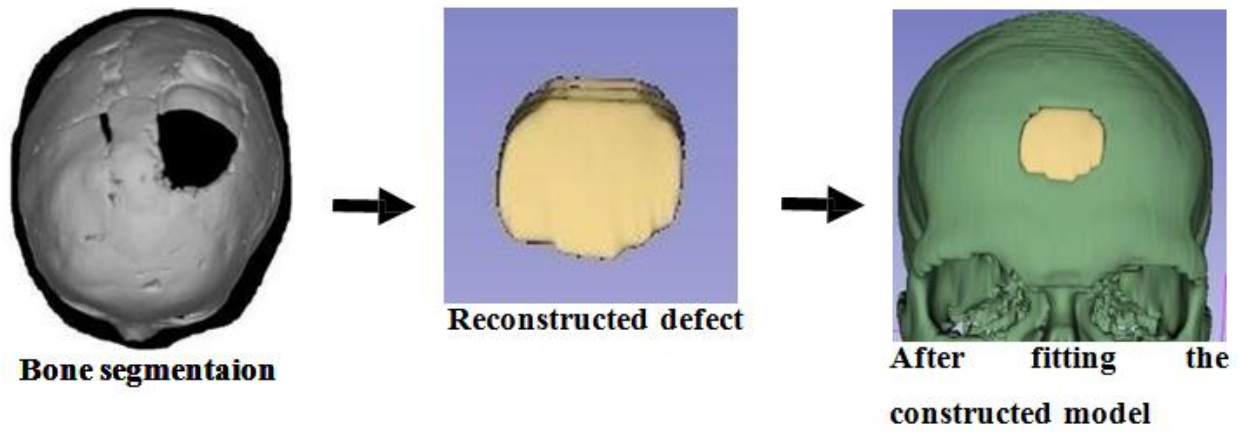
Figure 8. Bone segmentation using the algorithm VTK Python.The figure illustrates the bone segmentation from patient 1 dicom image.
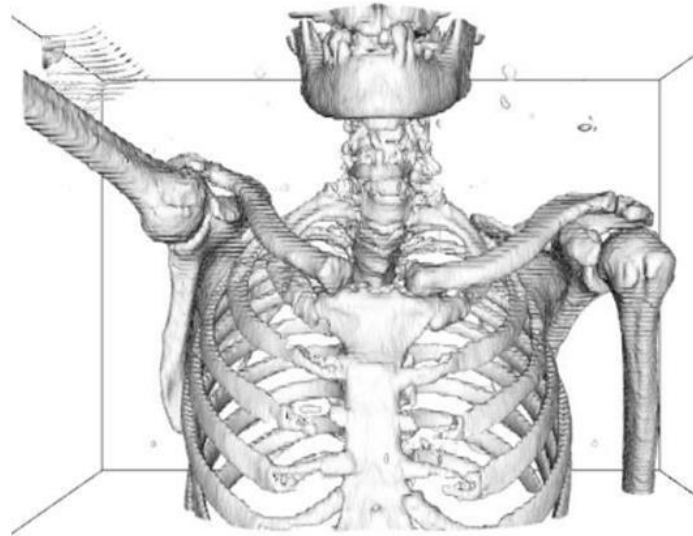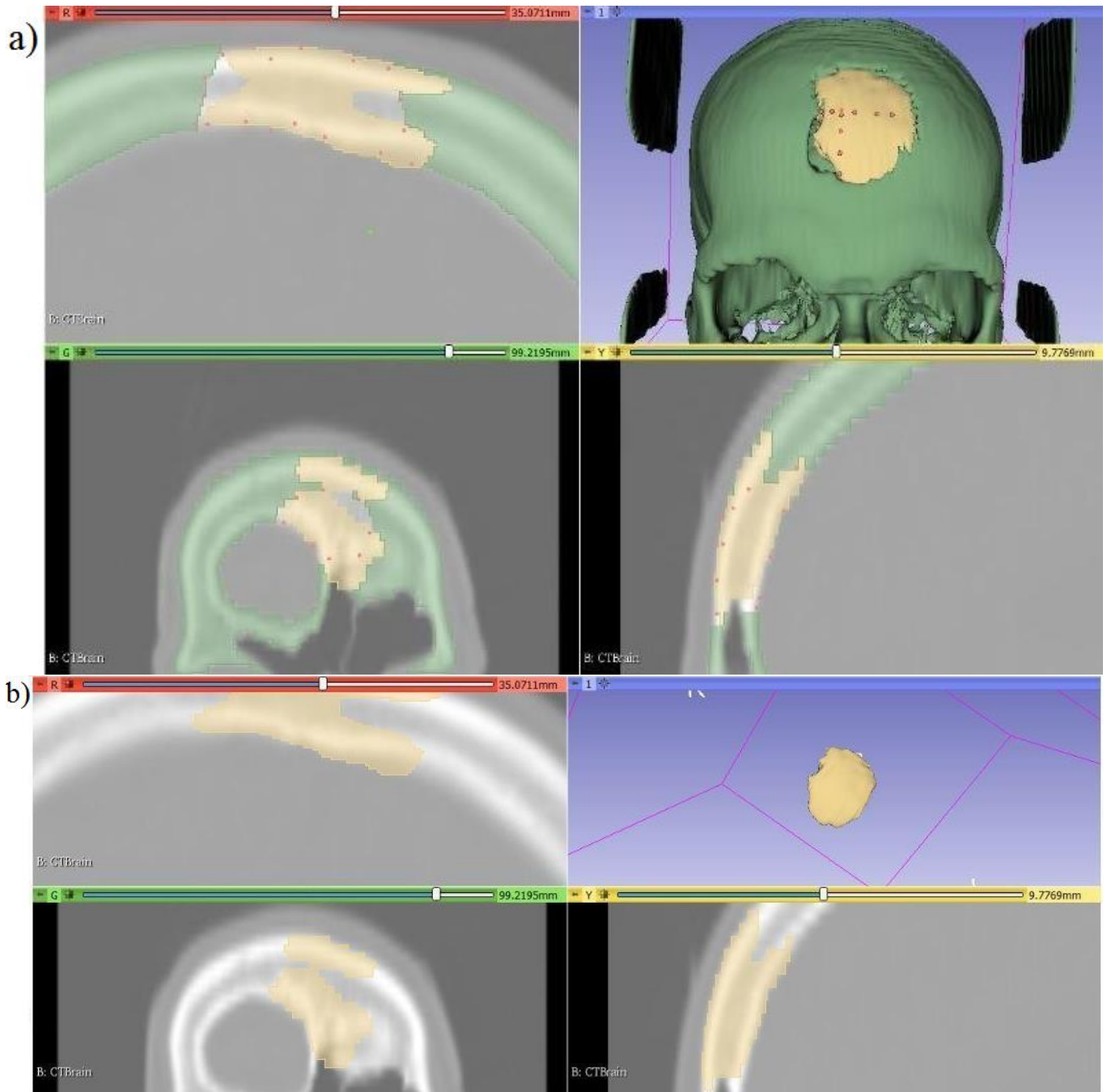

Figure 9. Reconstruction of the defective area using the 3D slicer (4.10.2) NVIDIA AI-assisted segmentation.

Figure 10. Pipeline for reconstructing bone defects.

Figure 11. (a) Reconstruction of the defective bone area using Nvidia AI-assisted segmentation available in the 3D slicer; (b) Volume of the constructed model.

CONCLUSION

Medical imaging is one of the most important tools in the field of diagnostics, which also assists surgical planning. Medical images can be obtained *via* different imaging modalities such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), Single Photon Emission computed Tomography (SPET), and Computed Tomography (CT). However, data processing issues are being reported in the presence of a large number of medical images, generating an enormous amount of data (slice resolution with 16 bits/voxels precision can be provided by a modern CT scanner). Various visualization libraries have been developed specifically for medical images, of which the Visualization Toolkit (VTK) is the most reliable standard. VTK is a cross-platform, and open-source library that is considered the main reason

for the rapid development of medical imaging tools that can be used for 3D computer graphics, image processing, and visualization.

Our aim was to develop a computational model to design 3D printed scaffolds using CT imaging to reconstruct actual bone defects. We present a successful method to model the bone defects using CT images utilizing two algorithms; Bag of feature method using MATLAB and using vtk python with NVIDIA AI assisted segmentation. This method can be used for reliable prediction of the scaffolds to be 3D printed using micro CT analysis and related algorithms to effectively minimize potential post-surgery complications associated with geometrical mismatches between the scaffolds and the defect.

The Nvidia AI-assisted segmentation is available in 3D Slicer, a popular open-source medical image visualization and analysis application. The tool is available in the Segment Editor module of the application. This study can be improved further by setting up our own segmentation server.

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