

3D Printing in Medicine: Application in Intracranial Tumours in Southern Nigeria

Abstract

Background

The pituitary gland is a small bean-shaped gland situated at the base of the brain and composed of three distinct histological parts. It produces several hormones that control other endocrine glands. Tumours affecting the pituitary —both adenomas and carcinomas— are neuroendocrine and are one of the most common intracranial tumours. Pituitary gland is a small bean-shaped gland situated at the base of the brain. Pituitary based tumors are neuroendocrine tumors affecting the pituitary gland. Imaging of the pituitary gland involves the use of computed tomography and magnetic resonance imaging. 3D reconstruction of CT imaging data from Ct images can be converted into 3D and turned into a living anatomical model converted 3D and then made into a live anatomical model using a 3D printer. The objective and aim of this study is to demonstrate, through the presentation of a series of three cases, that findings from cross-sectional CT scan and MRI images can be used to generate specific 3D printed specific models for patients and clinicians.

Methods

Patient specific models for three clinical cases were segmented using a segmentation application to isolate the mass and the bone. The process involved image acquisition from a cross sectional imaging to segmentation of the acquired DICOM image into 3D model followed by file and model correction for final print, this is then followed on to slicing with the selection of 3D printing material as well as appropriate settings, this is then concluded with the actual print, print accuracy and cost analysis.

Results

Segmentation of the region of interest took about 45 to 90 minutes with the majority of the time spent on segmentation of the pituitary. Printing of models was done into sections as the skull and mass were printed separately. The times required spanned from 20-40 minutes and 4-

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9 hours for the mass and skull base respectively. Print accuracy was less than 1.7mm with total cost of printing a model was less than \$50.

Conclusion

In this study we were able to show steps in 3D printing anatomical models from a computed tomogram of patients with brain lesions.

Keywords: 3D printing, accuracy, Digital Imaging and Communications in Medicine, intracranial tumours, accuracy, pituitary gland, segmentation, DICOM

Introduction

The pituitary gland is a small bean-shaped gland situated at the base of the brain and composed of three distinct histological parts. It produces a number of several hormones that control other endocrine glands. These hormones include, adrenocorticotropic hormone (ACTH), stimulating thyroid-stimulating hormone (TSH), growth hormone (GH), luteinizing hormone (LH), and follicle-stimulating hormone (FSH). Oxytocin and arginine vasopressin. Also released secondarily are oxytocin and arginine vasopressin. These hormones play a critical role in regulating several an array of physiological processes, such as including cardiovascular, metabolic and reproductive. [1]

The pituitary gland is located within the pituitary fossa with complex relationships. Inferiorly, it is bounded by the sphenoid sinus, superiorly, by the diaphragm sellae, laterally by the cavernous sinus, anteriorly clinoid processes and posteriorly by the posterior intercavernous sinus and dorsum sellae. [2]-(2).

Tumours affecting the pituitary —both adenomas and carcinomas—are neuroendocrine tumours— and are one of the most common intracranial tumours. [3] that primarily affect the pituitary gland. It is also one of the most common intracranial tumours. Pituitary adenomas are usually classified into micro and macroadenomas, the latter being defined by a size greater than 10 mm they are commonly categorised as microadenomas and macroadenoma. Macroadenoma are regarded as tumours more than 10mm or more while

microadenomas are less than 10mm in maximal width, while microadenomas are smaller than this. However, this differentiation is regarded as arbitrary.[4] However, this differentiation is regarded as arbitrary. (4) Studies show that pituitary adenomas are common and . They account for approximately 10% of intracranial tumours and 30-50% of all masses in the pituitary region masses(3,5). [3,5] Autopsy and radiology studies have shown that between 10% and 20% of all pituitary tumours may be incidental. [6]

(6).

In evaluating pituitary tumours, magnetic resonance imaging (MRI) is the preferred modality for assessing the pituitary gland and surrounding adjacent structures. Other alternative imaging strategies to aid visualisation are Positron Emission Tomography (PET) with Computed Tomography (PET/CT) and positron emission tomography with magnetic resonance imaging MRI (PET/MRI), which permit correlation of function and anatomy (7). However, incidental pituitary tumours are discovered on CT, leading to the use of MRI which further prompts use of MRI in evaluation in the evaluation. [7,8] (8).

Treatment recommendations for pituitary tumours range from no immediate treatment to medical or surgical treatment. However, surgical treatment is the mainstay of treatment. Treatment recommendations of pituitary tumours range from no immediate treatment, medical or surgical treatment. Surgical treatment however, is the mainstay of treatment (7). Surgical approaches like, Surgical approaches, such as the minimally invasive transsphenoidal approach, are considered which is regarded as safe, versatile, and effective in about 95% of pituitary tumours (9). Difficulties like such as incomplete resection may occur depending on various factors like such as tumour size of tumour and proximity to vital structures such as the neurologic structures, carotid arteries and the adjacent cavernous sinuses located adjacently. Surgery poses other risks. Mortality, which is the least lowest incidence accounting of them accounts for less than 0.5%, however but other major significant complications such like as CSF leakage, meningitis, ischemic stroke and intracranial haemorrhage can may occur.

~~Furthermore~~In addition, minor complications ~~like such as~~ sinus disease, septal perforations, epistaxis, wound infections, and hematomas also can occur.~~[7,9](9)~~

Treatment of pituitary tumours usually requires a detailed multidisciplinary approach to planning the patient's management. The multidisciplinary team (MDT), may comprise ~~of~~ clinicians from various disciplines, including endocrinology, neurosurgery, radiology and otolaryngology [ear, nose and throat (ENT)], to determine ~~the~~ suitability for surgery and inform the choice of surgical approach.

Three dimension construction of cross-sectional medical images involves ~~the use using of~~ stacked 2D Digital Imaging and Communications in Medicine (DICOM) images from cross-sectional imaging modalities like MRI and CT. DICOM images ~~is are~~ the leading standard in the medical imaging field~~(10)~~.~~[10]~~ DICOM images are converted to 3D computer-aided design (CAD) data. Out of the about 100 file formats of 3D CAD files used as native 3D data, stereolithography or Standard Tessellation Language (STL) file format is the most commonly used for 3D printing~~(11)~~.~~[11]~~ There are commercial and open source software packages ~~for the that~~ segmentation of DICOM images ~~to into~~ STL data, all of which run on a general-purpose personal computer (PC). Examples include 3D slicer, 3D view, Image J, Mimics, InVesalius 3, OsiriX lite, Seg3D, etc. However, some imaging workstations provided by companies (e.g. General electronics) that produce image scanners now have software available for converting DICOM to STL files~~(12)~~.~~[12]~~

3D printing systems come in various forms like Fused deposition modelling (FDM), Stereolithography (SLA), Digital Light Processing (DLP), Selective Laser Sintering (SLS), Selective laser melting (SLM), Laminated object manufacturing (LOM) and Digital Beam Melting (DBM)~~(13)~~. FDM printers/technology is currently the most popular 3D printing technology and ~~is~~ used in ~~both~~ affordable 3D printers and even 3D pens.~~13~~

Applications of 3D printing from cross-sectional images like MRI and CT have shown great importance in several surgical practices such as surgical planning, implant preplanning and

enhancing patient understanding of the condition and surgical process (14). Guidelines and applications of use of for 3D printing have been developed in clinical practice, including, maxillofacial, orthopaedics, cardiac and hepatobiliary, and other conditions where it may have a potential role in informing management. [14]

In this work, we aim to demonstrate that findings from CT and/or MRI cross-sectional images of several patients can be used to produce 3D printed patient-specific models. We showed the process involved in 3D printing a brain tumour. Lastly, we compared the accuracy of the 3D prints with the cross-sectional images acquired.

Methods.

Imaging

CT scans were acquired with GE CT scanners in radiological centre in southern Nigeria. Images were reconstructed using a 3D slicer. 3D slicer is a desktop software application for the visualisation and analysis of medical images and computing data sets. DICOM images were exported to a PC and then segmented to a 3D surface model. CT head of 3 patients were obtained with scanning parameters shown in table 1;

Table 1: Cases

Case	Age (years)	Sex	Slice thickness	Imaging findings
Case 1	25 years	Male	1.25mm	Contrast enhanced lobulated mass in the pituitary fossa with multifocal areas of hyperdensity of calcific attenuation. Mass is seen eroding anterior and posterior clinoid processes
Case 2	7 years	Female	5mm	Large calcified wedge-shaped mass merging imperceptibly with the pituitary fossa and the clinoid processes in the pituitary fossa. There is associated obliteration of the aqueduct of sylvius with resultant

				dilatation of the 3rd and lateral ventricles
Case 3	52 years	Female	3.75mm	Irregularly shaped contrast enhancing hyperdense solid mass with calcifications arising from the sella with an adjacent cystic component extending into the suprasellar space. The mass is infiltrating the sphenoidal sinus, eroding into the sphenoid bone, part of the right petrous, temporal bone as well as the anterior and posterior clinoid processes bilaterally but worse on the right.

Image segmentation and model preparation for 3D printing.

The CT DICOM images were collected and loaded onto the 3D slicer software. The skull was segmented from the CT using voxel Hounsfield unit (HU) values between 100 HU and the maximum HU in the image. Small floating structures within this segmentation were removed using the 'Islands' and 'scissors' tool. In the segmentation of the tumour, two segments were used- that of the tumour and other tissue. This tumour was then selected using the 'paint' tool. The paint seed was placed within the tumour and on the normal tissue around the tumour. The 'grow from seeds' is then selected to initialise automatic region growing and then show a 3D presentation of the tumour. The resultant segmentation is refined by painting the areas not selected by the automatic region growing. Some smoothing is done to reduce the segmented surface. The structures were smoothed using a median smoothing filter of 3 mm. The image generated is then reassessed to check if the edges of the tumour are covered. The final segments are then exported into an STL file with a scale of 0.3 to 0.5. The final STL file was transferred to a creality slicer application which converts the 3D object model to specific instructions for the printer. The converted version from the STL is processed in g-code format used by the fused filament 3D printer. The 3d slicer parameters used include an infill of 10-20%, extrusion thickness of 0.2mm and presence of support as well as brim for adhesion to the print bed. Minimal support material was however used to reduce print time and need for post

processing of the 3D printed models. Printing was used with a consumer-available 3D printer, Creatlity Ender 3 pro v2. PLA filaments were used to print using a layer height of 0.2 mm and a 0.4 mm nozzle.

Cost analysis

The cost of production of each model was divided into two, the cost time spent at segmentation and cost of PLA material used to print the model. The cost of PLA material was calculated from the purchase price of the filaments and weight of the final 3D printed model. The personnel cost was estimated to be about \$23 per hour.

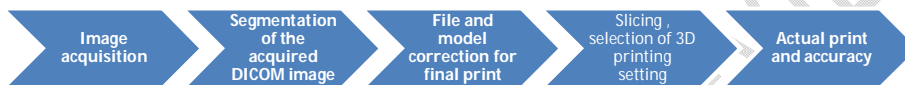


Figure 1: Steps/workflow in developing a 3D print from acquired image **Results**

Model preparation and printing

Segmentation of the region of interest took about 45 to 90 minutes with the majority of the time spent on segmentation of the pituitary tumour. This was made easy with the IV contrast enhancement and calcifications of the mass. Segmentation of the bony structures required using a near automated thresholding technique.

Printing of models was done into sections as the skull and mass were printed separately. The times required spanned from 20-40 minutes and 4-9 hours for the mass and skull base respectively.

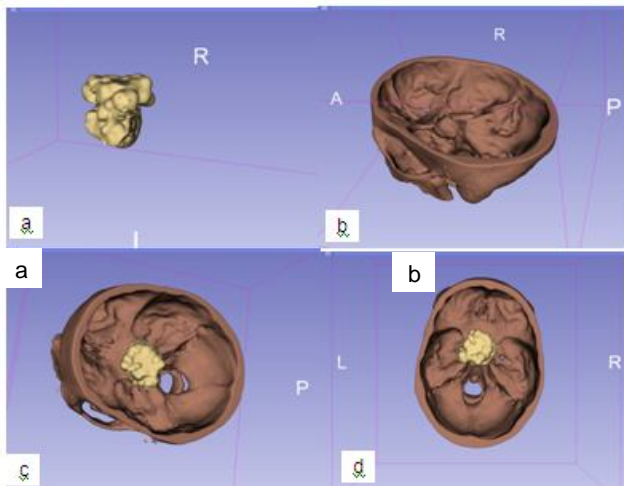
Table 2a: Print accuracy of 3D printed anatomical model

Case	Mass (3D printed) (mm)	Mass (CT image) (mm)	Mass (3D printed with scaling) (mm)	Difference (mm)
Case 1	18.3	35.0	36.6	1.6
Case 2	21.7	44.3	43.7	0.6
Case 2 (dilated)	11.1	22.7	22.2	0.5

ventricles)				
Case 3 (Solid component)	9.0	30.9	30.0	0.9
Case 3 (Cystic component)	8.3	27.8	27.6	0.2

Table 2b: Print accuracy of 3D printed anatomical model (skull base)

	Skull (3D printed) (mm)	Skull (CT image) (mm)	Skull (3D printed with scaling) (mm)	Difference (mm)
Case 1	56.8	114.8	113.6	1.2
Case 2	65.0	130.5	130.0	0.5
Case 3	38.0	128.0	126.7	1.3



c

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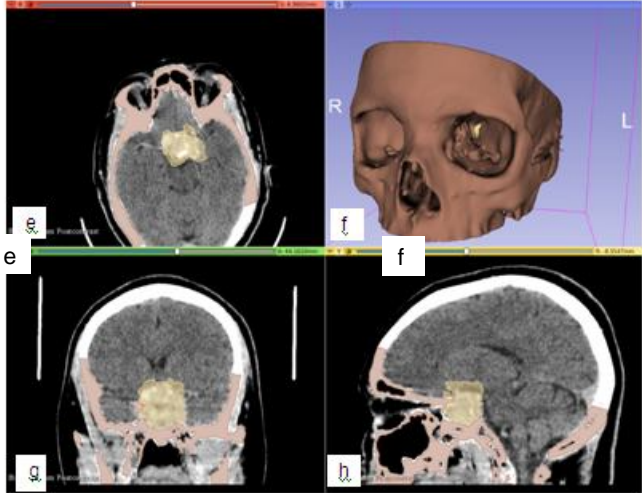
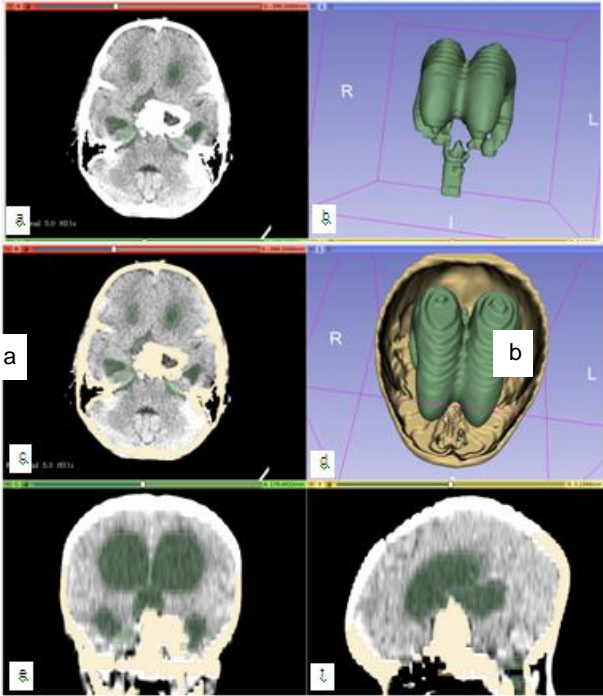


Figure 2: Case 1a-h. Lobulated mass in the pituitary fossa with 3D volume rendered images; the mass separately (a), pituitary fossa without the mass (b), mass in situ in skull (c-d), facial bones (e, g), and fragmentation of mass on orthogonal CT stacks (e, g & h).



c

d

Figure 3: Case 2 a-f: Lobulated predominantly calcified mass in pituitary fossa. Axial, coronal and sagittal CT Images showing dilated ventricles and calcified sellar mass (a, c, e & f). Segmented stacks with 3D volume rendered image of the dilated ventricles and skull (b & d).

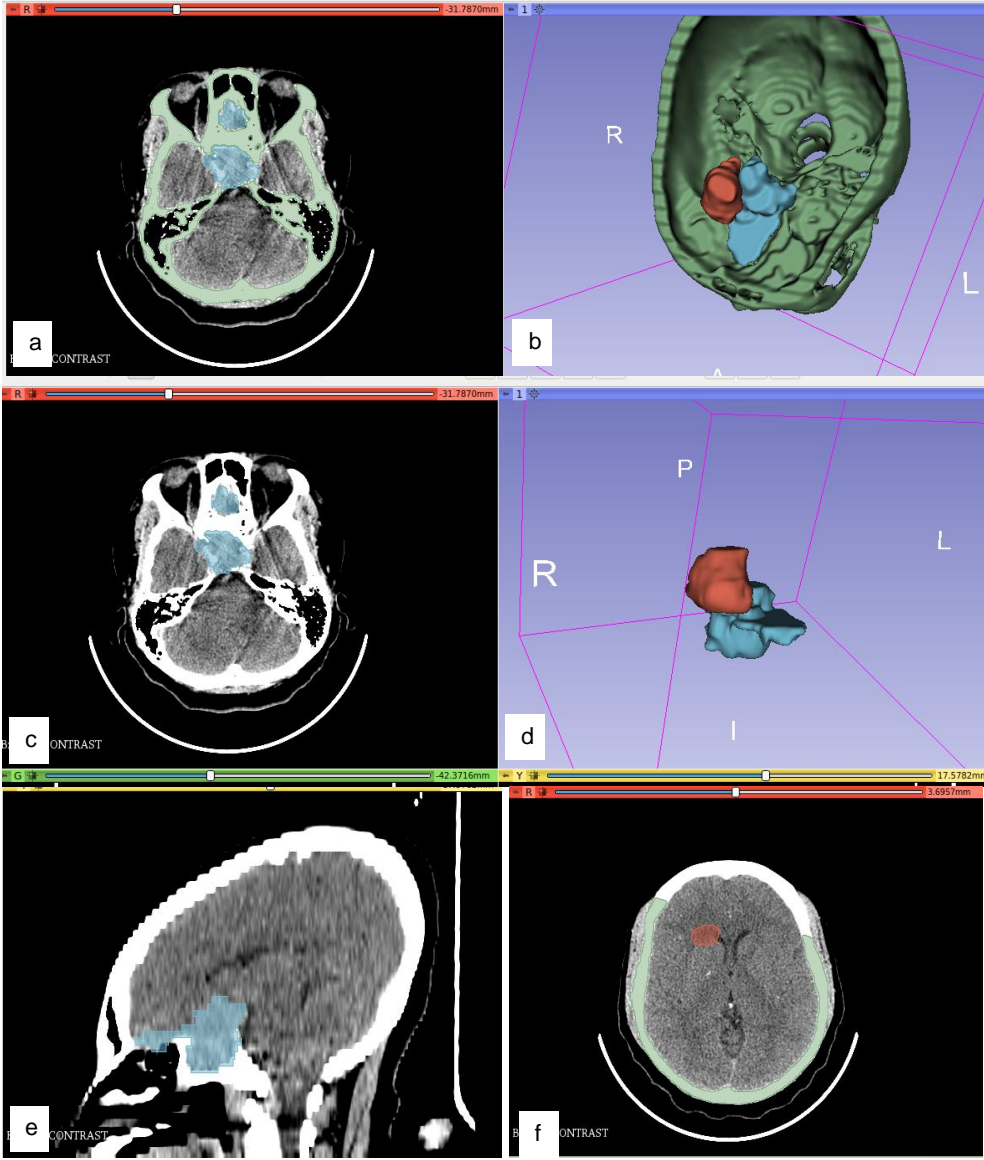


Figure 4 Case 3 a-f: Axial and sagittal Images showing irregularly shaped solid mass (blue) with calcifications arising from the sella with an adjacent cystic component (brown) extending into the suprasellar space (a, c & e) and into the right frontal lobe base (f) which was not so apparent on the CT stacks. Segmented and 3D volume rendered image of the mass and skull (b) and mass separately (d).



Figure 5: Case 1 Showing 3D printed loculated mass, skull base and with mass within the pituitary fossa

UNDER REVIEW

REVIEW

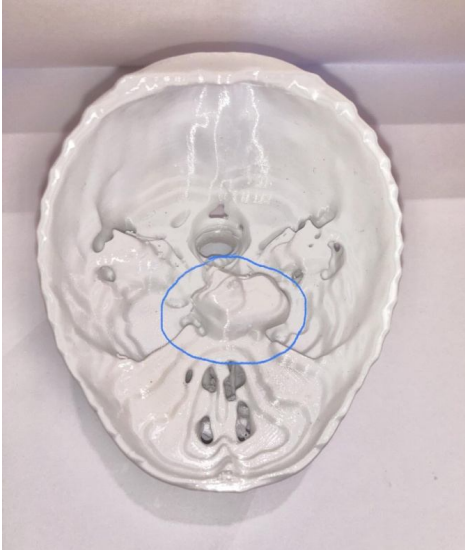


Figure 6: Case 2 Showing dilated ventricles, skull base and the calcified mass merging with the pituitary fossa (blue circle)

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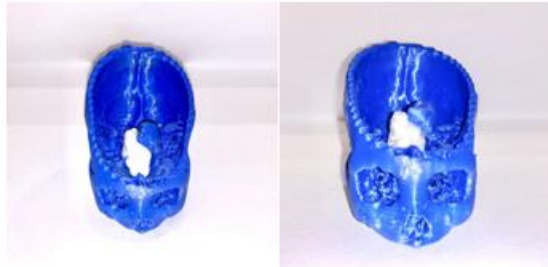


Figure 7: Case 3 Showing 3D printed loculated mass, skull base and with mass within the pituitary fossa

Table 3: Time of printing, segmentation and cost analysis of each model

Case number	Time of segmentation (minutes)	Printing length (hours)	Amount of PLA filament used (grams)	Cost analysis of PLA filament used (\$25/kg)	Personnel working cost	scaling
Case 1	45	9.25	36	\$0.75	\$23	0.5
Case 2	55	9	53	\$1.1	\$23	0.5
Case 3	90	4.25	16	\$0.32	\$46	0.3

Discussion

In this study, we identified the 3D printing workflow can be divided into five steps, similar to previous studies(15) and the stages were similar. This involves image acquisition from a cross

sectional imaging to segmentation of the acquired DICOM image into 3D model followed by file and model correction for final print, this is then followed on to slicing with the selection of 3D printing material as well as appropriate settings, this is then concluded with the actual print and print accuracy.

Segmentation of the structures of interest, particularly the tumour involves the use of drawing tools to manually segment the tumour(10) however, the process was aided by use of contrast enhanced images where the tumours tend to stand out due to contrast enhancement, and the presence of calcification as well made segmentation easier with use of semi-automatic tools like thresholding. Use of artificial intelligence and deep learning approaches for automated classification and segmentation of head and neck cancers and brain tumours have been described and this can make this process automated in the future(16). This approach is however novel and was not employed in this study.

Bone was a very easy structure to segment when using segmentation tools and Hounsfield units(10).. The bone is the most important aspect of the final model as it gives the relation of the tumour with the skull vault. It also shows infiltration by the tumour. In this study, we were able to identify bony destruction caused by the lesion and identify the lesion in relation with the skull.

The time it took to segment models differed depending on the complexity of the tumour in terms of its margins and borders. This ranged from 45-90 minutes, similar average times of segmentation has also been described in several studies(7,17) Use of FDM printers made it possible for models to be printed immediately as soon as the STL file models were available.

This is because FDM printer are commonly commercially available printers and were made available

Print accuracy was a consideration following prints of the models. It was observed that the print accuracy of all the anatomical models was less than 1.7mm (table 2). This is however not entirely surprising as FDM printers generally have the print accuracy of +/-0.5mm with mean errors of 0.44% (18,19).

The range exhibited could be from user bias in measuring, scaling and also slicing thickness of images which lead to step ladder artefacts could have influenced measurement. The total time from segmentation of image to 3D printing took an average of 8 hours. This further can give the impression of the possibility of having point of care 3D printing of models that can be made available within 24-72 hours depending on the complexity of the case and skills involved.

Cost analysis is an important consideration especially if this is to be considered in a clinical setting. Cost analysis spans from time spent in development, cost of materials and cost of 3D printers. This can be greatly influenced by the nature of lesion size, shape and complexity in terms of mass infiltration. Another important consideration is the cost of the printer. But, considering this is a fixed item, the cost of the printer is not considered. The cost of each item is estimated during slicing which estimates the amount of PLA filament to be used in grams and metres. We were able to show that raw material printing cost is dependent on the scale of printing. In this study, the costs of PLA filament used per model was less than \$1.2. In terms of personnel cost for segmentation, the time spent would determine the cost of segmentation

with cost between \$23 and \$46 making the total cost less than \$50 per model (table 3). This level of cost effectiveness has been described in similar studies(7,17)

Conclusion

In conclusion, we have shown it is possible to segment DICOM images of pituitary lesions and 3D print using an FDM printer with less than 1.7mm print accuracy. With this, we believe this can pave the way for point of care 3D printing for patients and clinicians when needed. We have also done cost analysis and shown it can be cost effective as well.

Limitations of study.

One major limitation in this study was poor contrast enhancement of carotid and cerebral arteries. Good segmentation of the cerebral arteries would have given more view on tumour relationship with surrounding vessels. The use of one imaging modality in this case, a CT scan machine was considered as a limitation in this study. Other imaging modalities like MRI would have helped give a further and more detailed assessment of the tumours. Also, this study was based on just 3 clinical cases, use of more cases would have given more insight on factors that may affect accuracy.

A comprehensive study modelled on this work should be the obvious next steps in making it very relevant to the clinical practice especially in the sub-Saharan Africa.

Consent and ethical approval

As per international standard or university standard guideline ethical approval has been collected and preserved by the authors.

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