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Additive manufacturing: a growing platform to replace, reduce and refine animal experiments

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Abstract: Replacement, Reduction and Refinement (3Rs) are the bedrock of animal experiments and additive manufacturing (AM) fortifies these principles. To evaluate the accuracy of 3D models, we built skeletal models of rabbit head, based on Micro-Magnetic Resonance Imaging (µMRI) and Micro-Computed Tomography (µCT). Data was segmented using a computer software and the reconstructed stereolithography file was printed in 1:1 scaled model using a polyjet printer. Point-based part comparison analysis (PCA) was performed to gauge its dimensional accuracy. The results displayed that AM-workflow is an accurate process for reproducing life size skeletal models, however support material cleaning requires further research.

I. Introduction

The conventional approach of animal dissection is becoming an alarming concern in increasing the load on animal experiments, ethical approvals and amplification of costs [1]. Thorough anatomical knowledge is applied by biomedical engineers and researchers to develop neuromuscular devices, surgical protocols and implants [2,3]. In this aspect, past decade witnessed a brisk paroxysm of 3D printing applications [4–7]. The objective of our work was to create a tangible rabbit head model with Polyjet technology. Rabbits are useful in pre-clinical studies owing to the close resemblance to humans [8,9].

II. Material and methods

We scanned two sacrificed New Zealand rabbits, each for multimodal image acquisition of the head using µCT (Siemens Inveon® µCT, Siemens Medical Solutions) with a voxel size of 97 µm; and µMRI (BioSpec® 94/30USR MRI, Bruker, Bruker Medical, Ettingen, Germany) with a pixel size of 439 µm and a slice thickness of 1.45 mm and analyzed one head in detail. Prior sacrificed rabbits from an ongoing study (approved by Ethics Commission, Medical University of Vienna, Austria) in the department of Biomedical Research, Medical University of Vienna, Austria, were utilized for this study eliminating the need for ethics approval. µMRI only served as an additional tool regarding spatio-temporal arrangement and information of soft tissues and cartilage (Fig. 1A). Imaging data obtained as DICOM files was rendered and segmented using Mimics USL 21.0 software (Materialise, Leuven, Belgium). Design optimization and modification of the scanned data on mesh level, was done using 3-Matic 13.0 software (Materialise, Leuven, Belgium) (Fig. 1B) and topologically optimized models were constructed digitally. A combination of VeroPureWhite and Tango+ were pegged as the most appropriate materials, based on the maximum ultimate strength to mimic bone and cartilage (Fig. 1C). Cleaning was done by manual removal of support material (SUP 706) for gross parts followed by waterjet device. The model was then placed in 1-2% sodium hydroxide (NaOH) solution for 15-20 minutes and cleaned again with waterjet.

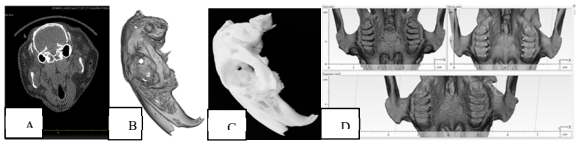

Figure 1: Pictoral representation of workflow- A:µCT, Figure B: Rendering of STL, C: Additive manufacturing, D: PCA Analysis(white dots represent the anatomical landmarks)

To analyze the dimensional accuracy of the AM model, a µCT scan was done using the same device. The STL file was used to perform point-based part comparison analysis (PCA), an analyse tool available in 3-Matic 13.0 software (Fig. 1D). In this analysis, palatal cusps of all maxillary molars in the original STL were overlapped with the model STL and both visually and analytically evaluated. For a detailed evaluation of the results from the point-based part comparison analysis, segmentation of the failure range was performed, which is described in Fig. 2A. This function classifies the reconstructed AM model entities into failure ranges from minimum to maximum, defined by increasing grey scale (grey to black). Based on the segmentation analysis, the reason for the failure of each entity was postulated.

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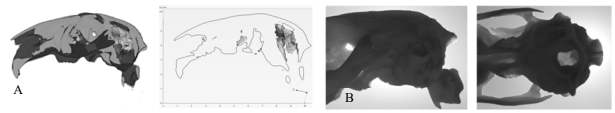

Figure 2: A: Segmentation of the failure during superimposition, B:Reconstructed AM rabbit skull model in sagittal (left) and ventral (right) view confirming the presence of support material through the opaque areas, corresponding to the highest failure.

III. Results and discussion

All the anatomical landmarks on the STL model were accurately replicated on the 3D printed model with a printing resolution of 600 dpi (42.3 µm) in xy-plane and a layer thickness of 30 µm in z-direction (Fig. 1C). The results from PCA were transformed into a histogram with the total number of entities in the AM model taken into consideration by the software function, on the y-axis, and the failure range (range of mismatch with the original skull STL in mm) on the x-axis (Fig. 3B). Failure range varied from 3.4 µm (light grey surface) to 6.1209 mm (black surface) with a mean failure range of 0.4821 mm. The total number of entities and their failure range is shown in the Table 1. From this analysis, it was interpreted that 72,821 entities, approximating to 80% of the total (shown in green) displayed the mean failure of 0.4821 mm. Thus, the accuracy of the AM model was shown to be 80% within a range of 0.0-0.5 mm (Table 1). Segmentation analysis of the STL file from the AM model was done to segregate the analysis result in the defined range (Fig. 3). Segmentation analysis showed the detailed evaluation of the failure range of 0.0 to 8.7 mm in the respective surfaces and entities. Direct images of the reconstructed AM model were taken in natural light to confirm the results from the segmentation analysis. The opacity in the hollow regions of the model was due to the presence of support material. Failure part analysis shows the involved parts of the maximum failure rate (2.0-8.7 mm, i.e., B to D), based on residual support material (SUP706). The detailed analysis of the reconstructed AM rabbit skull model shows that the AM model reached an accuracy of 52% in a range of 0.0-0.2 mm and 80% up to 0.5 mm failure (Table 1). For active implants like stimulation units and drug pumps, the failure rate of 0.0-0.5 mm is acceptable and hence a higher probability (80%) of usage of these models is suggested by our study.The analysis shows that the high failure rate (2.2-8.7 mm) was based on the residual support material which was used during the printing process (SUP 705 and 706).
The support material was encapsulated by the replicated cancellous bone. The newer water soluble support materials (SUP 707) could be an alternative to the NaOH-soluble SUP706. In a nutshell, we can display that additive manufacturing based on three-dimensional imaging modality like CT scan is a good platform for reduction of animal experiments.

IV. Conclusions

In conclusion, 3D printing serves as the glue that bonds and focuses many of the multidisciplinary approaches as realized in our study. The development of intelligent neuroprosthetic concepts will continue unabated using 3D printing. Our workflow shows the possibility to include this technology inside a quality management program to prove the accuracy of replication via polymer models.

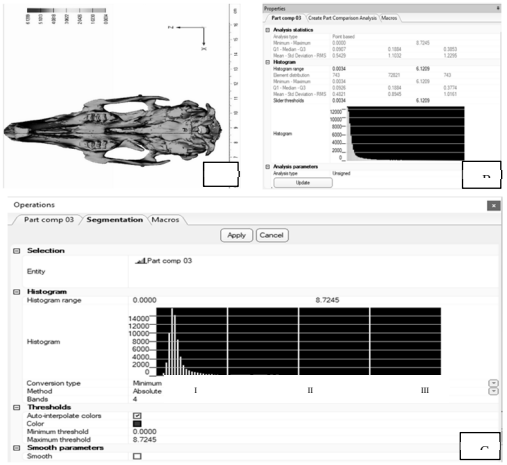

Figure 3: A: STL-model; B,Graphical interpretation of the results from segmentation analysis; C, Histogram of segmentation analysis of failure categorized into 4 ranges in increasing order - I,II,III, and IV. The. Maximum entities lie in range 1

Table 1: Table showing the accuracy of the AM model compared to the original STL data set after superimposition and part comparison analysis

Percentage of entities	*Failure range (mm)*
27%	*0.0-0.1*
25%	*0.1-0.2*
16%	*0.2-0.3*
8%	*0.3-0.4*
4%	*0.4-0.5*
8%	*0.5-1.0*
7%	*2.0-8.7*

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Author's statement

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