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To the Editor,

Please find attached our itemized response to the editorial comments and reviewers 1-3 for our manuscript (55340) titled "Sub-Surface Laser Engraving (SSLE) of Glass Crystals as a Medium for the Display of Biomedical Tomographic Imaging Data and Associated Labels." We believe the review process has served to strengthen the manuscript and we are excited to move forward with publication in JoVE.

Sincere regards,

W. Matthew Leevy, Ph.D.
Research Associate Professor
Director, Biological Imaging

Editorial Comments:

1) Please note that section 8 has been highlighted and we do intend to show the crystal engraving process in the video.

2) Line 281 – "profession" has been changed to "professional"

Line 525 – "diseases" has been changed to "disease"

3) Visualization – The overall software approach uses PMOD (www.pmod.com) to 3DSlicer (slicer.org) to Netfabb (netfabb.com). We are not running scripts on these platforms.

4) Two comments:

a) CT Imaging Reference: Please note that reference 5 has been added.

Hsieh, J. Advanced CT Applications. In: *Computed Tomography, Second Edition: Principles, Design, Artifacts, and Recent Advances.* Chapter 12, Section 1, doi:10.1117/3.817303.ch12, (2009).

b) 3.2 Edited to "typed anatomical labels"

5) Commercial branding removed.

6) "Outstanding" changed to "useful"

<u>Reviewer 1:</u>

No changes requested.

<u>Reviewer 2: Major Concerns</u>

Comment 1: The authors agree with the reviewer and this sentence has been deleted.

Comment 2: To address the reviewer's concern, the sentence has been edited such that it reads "…materials, especially for consumer-grade machines,…"

Comment 3: This comment objects to the "protocols section as presented." The intent of this manuscript is to provide a protocol, in line with the overall mission of JoVE. Further, we believe this work will be of significant interest to the biomedical imaging community at large since SSLE is not a widely known medium for data visualization. Further, we believe JoVE is a solid match

for this report as the video presentation of each anatomical crystal will highlight their visual impact.

Comment 4: This sentence has been edited for clarity as follows:

"2.1 Open each DICOM data set (comprised of all image slices) using the 'Load DICOM' in the 'View' setting of the image processing software."

Comment 5: The reviewer addresses two important concepts in this section: The number of faces in a given surface, and the point size (density) that is inscribed into the crystal. To better address this question, the following paragraph has been added:

Two additional factors must be considered when performing SSLE of anatomical data: the number of faces within a surface map, and the size of each point that is lasered into the crystal. These factors affect the number and size of the points that will absorb incident light and thus potentially enhance or detract from a given SSLE visualization. First, the number of faces, which is directly proportional to the number of points in 3D space, will influence both the overall resolution and "brightness/contrast" of the displayed model. In each of the examples presented herein, the completed STL file was reduced to 100,000 faces without apparent degradation of the resulting crystal product, regardless of size or magnification. The overall brightness/contrast was also acceptable using this approach. The 100,000 value is the safe range for the engraver used as not to overtax the software and hardware. However, in some cases, additional faces may be needed to properly display a given data set, and these files may considered experimental until successfully completed. In addition, the size of each point that is "burned" into the crystal may be tuned via the voltage and "density" input values of the engraver to enhance the output brightness contrast. In the present cases, default values of Voltage: 8.5 and Density: 0.2 were selected. While these values represent a starting point, they may be altered in a trial and error fashion to improve data visualization as needed.

Comment 6: The reviewer's main concern is "novelty." We believe the use of SSLE to visualize biomedical imaging data is relatively unknown within the clinical and pre-clinical imaging communities. As the reviewer notes, we have striven to include scale bars and anatomical labels to bolster the overall scientific output of the tomographic data. Overall, this manuscript would appear to be a great match for JoVE since it is difficult to convey the visual impact of the SSLE data in a 2D static image.

Comment 7: To address this comment, the “prices of material vary greatly” has been deleted. As an advantage to SSLE, we have simply stated that it has a “lower relative material cost per volume.”

Reviewer 2: Minor concerns

Comment 1: “Difficule” corrected to “difficult.”

Comment 2: The Advantages/Disadvantages table is labeled.

Comment 3: The concluding paragraph comments on the overall utility of the SSLE anatomical crystals, with the education benefits arising from interacting with the data in the glass medium.

Reviewer 3: No major concerns

Reviewer 3: Minor concern

Line 89: “leveraged” has been changed to “used”