Project 15 Proposal:	Mouse Segmentation and Optical Properties for BLT
Date:	February 25, 2016
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Topic and Goal

The topic of this project is bioluminescence tomography (BLT), and specifically its application in localizing light sources in a mice for purposes of aiding in soft tissue targeting. The aims of this project are threefold:

1. To gather reported literature values of the optical properties of mouse organs and evaluate their distribution.
2. To produce a means of expediting the segmentation of cone beam computed tomography (CBCT) images of mice.
3. To experiment with BLT reconstruction incorporating information about the spatially varying distribution of optical properties in the mouse.

Statement of Relevance

CBCT is used in the Small Animal Radiation Research Platform (SAARP) to guide irradiation; however its utility in localizing targets with low contrast and small targets in soft tissue could be improved (1). The implementation of BLT allows an alternative means of determining the location of the internal source, provided it is bioluminescent. Use of BLT augments the research value of the SAARP, supporting its usefulness for preclinical radiobiological study. In earlier work involving the SAARP, BLT reconstruction was executed under the assumption of the mouse body's optical homogeneity; optimal properties were culled from literature and applied to all specimens (1). The incorporation of information about the spatial distribution of optical properties in the mouse body, even if approximate, could potentially support accuracy of the BLT reconstruction and perhaps yield greater robustness against dependence on target location.

Technical Summary of Approach

To achieve the first aim, data from the literature set will be tabulated and evaluated for mean, median, and standard deviation of given values for each organ. In preparation for incorporating this information into the BLT implementation, I will learn the normal workflow to run the BLT reconstruction without segmentation, as well as in simulation condition. After modification of the BLT Matlab code to incorporate organ specific optical properties, the modified code will be tested against a virtual source in the mouse CBCT.

To achieve the second aim, a set of CBCT images for mice will be manually segmented. The manual segmentations will be validated by a mentor's inspection. Using the elastix registration software package, different parameters for non-rigid registration will be tested to best match a subject mouse to each specimen in the atlas set; the transformation parameters will be retained and applied to the segmented images (2, 3). Once all the manual segmentations have been registered to the coordinate system of the new subject image, the multi-classifier decision fusion strategy will be used to produce the final segmented output; i.e., each voxel in the subject image will be labeled based on the most common label of the transformed segments occupying the same voxel space (4). Validation of the results will be done using metrics such as mean squared difference or normalized correlation coefficient.

For the third aim, a light source will be implemented in a mouse organ and reconstructed using either the manually or automatically segmented image, along with information regarding optical properties of each volume in the image. Assessment of BLT results will be performed by comparison of the light source center of mass as shown in CBCT versus the BLT reconstructed center of mass. Different optical property sets will be used in reconstruction to determine the relative strengths of each set.

Deliverables

Minimum Deliverables

- Tabulate literature values for optical properties
- Manually segment mouse images for atlas and simulated source
- Modify Matlab code to incorporate organ specific optical properties
- Test code under simulation conditions

Expected Deliverables

- Workflow for registering new images to atlas set using elastix
- Matlab code for multi-classifier decision fusion strategy

Maximum Deliverables

- Perform BLT experiment on implanted light source in specific organ
- Determine optimal optical property value sets for reconstruction

Key Dates

Key Milestones Highlighted	Week of:										
	February		March				April				May
	21	28	06	13	20	27	03	10	17	24	01
Read Elastix Manual (2-3)											
Read Core Literature (5-13)		1									
Project Plan + Presentation											
Read BLT documentation											
Run BLT on Sample Images			2								
Seminar Presentation											
Manual Segment Atlas Set											
Checkpoint Presentation											
Second Literature Round						3					
Modify BLT code											
Test BLT in Simulation								4			
Try Elastix Parameters											
Multi-class decision fusion											
Experiments with new sets										5	
Final Exam + Poster Session											

1. 3/5: Finished tabulating core literature results and main reading phase.
    - Ready for seminar presentation for week of 3/06
2. 3/12: Able to execute existing BLT workflow and begin modification
3. 3/27: Modified BLT code to incorporate optical properties information
    - Manual segmentations for atlas completed
    - Finished optical property data gathering
    - Ready for checkpoint presentation for week of 3/27
4. 4/16: Tested modified BLT with light source simulation
    - Decided on Elastix registration parameters

5. 4/30: Finished experimenting with reconstruction on new data from implanted sources
   - Ready to produce final report and presentation

Dependencies

Resource	*Status*	*Comment*
Mouse image set for initial BLT practice	Received	
Mouse image sets for atlas + experiments	Unknown	To be discussed w/ mentor 2/29 Digimouse alternative/complement (14,15)
Matlab source code	Received	
SAARP/BLT workflow documentation	Received	
Elastix registration software	Installed	
Nirfast light transport modeling software	Received	

Management Plan

Weekly meetings with mentor

All changes to BLT code to be done on local copy, with documentation of modifications

Preliminary Reading List

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9. Cheong, W., Prahl, S.A., & Welch, A. J. (1990). A review of the optical properties of biological tissues. *Quantum Electronics, IEEE Journal of, 26*(12), 2166-2185.

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11. Sandell, J.L., & Zhu, T.C. (2011). A review of in-vivo optical properties of human tissues and its impact on PDT. *Journal of Biophotonics, 4*(11-12), 773-787.
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13. Welch, A.J, Gemert, M.J.C. Optical-thermal response of laser-irradiated tissue. Dordrecht: Springer; 2011
14. B. Dogdas, D. Stout, A. Chatziioannou, RM Leahy, Digimouse: A 3D Whole Body Mouse Atlas from CT and Cryosection Data, Phys. Med. Bio, 52: 577-587, 2007. http://dx.doi.org/10.1088%2F0031-9155%2F52%2F3%2F003
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