An AI approach for automated and noninvasive in vivo liver sizing in mouse models

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1 Background

GOAL: increase the efficiency and quality of *in vivo* ultrasound liver imaging studies using artificial intelligence (AI) to segment the liver.

RATIONALE: Why use AI to segment livers from volumetric images?
1. Throughput: AI algorithms can process a 3-D image in seconds, compared to minutes for a human. This reduces the burden of analysis.
2. Repeatability: The AI model will always produce the same result for a given image, eliminating any issues related to inter-user variability.
3. Training: Even a novice user can produce reliable results, eliminating the need for expert personnel.

2 Imaging Methods

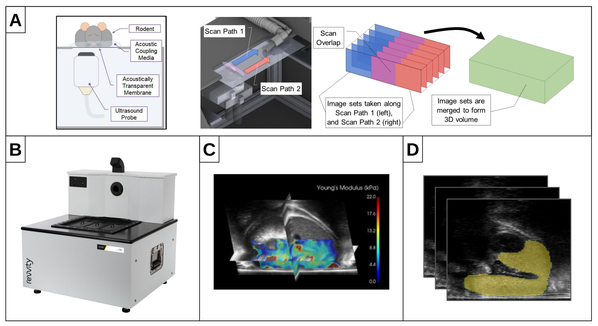

Figure 1: Schematic overview of image acquisition approach.
A: Rodents are placed on the ultrasound instrument in prone position and imaged from below via robotically controlled raster scan. Raw 2D frames are reconstructed into 3D volumes.
B: Photograph of Vega ultrasound in vivo imaging system.
C: Screenshot of multi-modal 3D B-mode and Shear Wave Elastography scan of a mouse liver in orthoslice view.
D: Screenshot showing output of AI-assisted 3D liver segmentation (yellow outline). Segmentation is used to quantify liver volume.

3 AI Training Methods

Data from various preclinical studies targeting the liver were collected and labeled with ground truth regions of interest (ROIs), which were produced using SonoEQ™ (Revvity) by expert readers. 522 images were divided into training and validation subsets using an 80-20 split. An additional unlabeled dataset (N=148) from a separate study was held out for further evaluation.

We trained a modified U-Net model to predict volumetric ROIs of the liver on the training subset of data. Our training infrastructure used PyTorch and the MONAI framework. All models were trained on an NVIDIA RTX 3090 GPU.

4 AI Training and Test Data

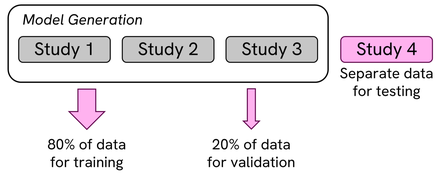

Figure 2: Simplified diagram of dataset split for training, validation, and testing. In total, Studies 1-3 comprised 522 images, 80% of which was used for training with the remaining 20% held out to measure validation performance. The model with the best validation accuracy was evaluated on a separate test study of 148 mice never seen by the model.

5 Validation Representative Images

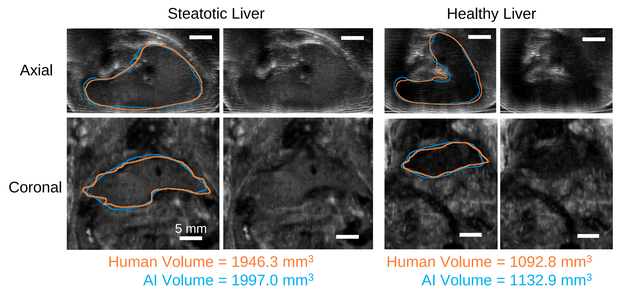

Figure 3: Representative images and ROIs for two mice from the validation dataset that was held during training. Human annotations are orange, while AI annotations are shown in blue. The example on the left shows a relatively large, steatotic liver, while the image on the right contains a much smaller liver from a healthy animal. The model generalized well across the different phenotypes present in the dataset.

6 Human vs. AI Comparison

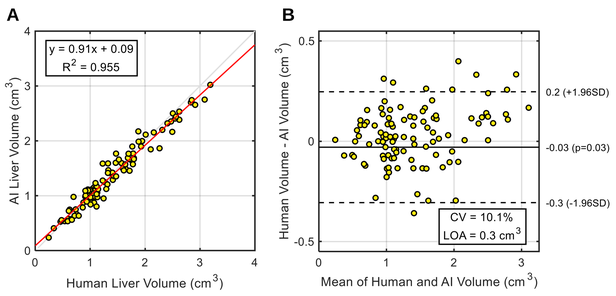

Figure 4: Examining agreement between human and AI liver volume measurements. A) linear regression analysis reveals a strong correlation between the AI-predicted volume and ground-truth (human annotated) volume, R^2=0.96. B) Bland-Altman plot shows that the AI model has a slight bias of -0.03 cm^3 and a limits of agreement of +/- 0.3 cm^3.

7 Independent Test Studies

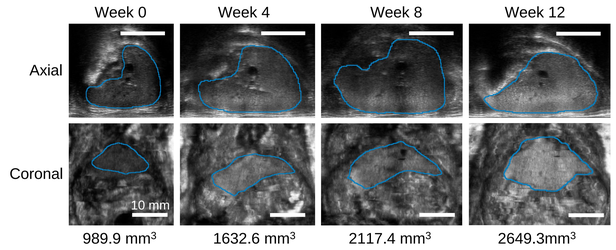

Figure 5: Representative images of one of the mice that was not used for the AI model development over time (Study 4). The AI-generated ROI can be seen in blue.

8 Automated Longitudinal Liver Volumetry

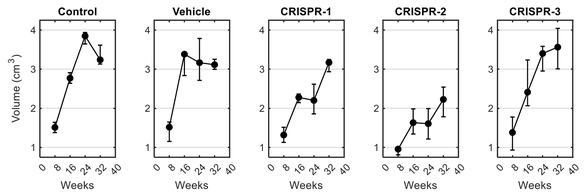

Figure 6: AI-measured longitudinal progression of liver volume over 32 weeks in mice fed GAN diet with CRISPR treatment. Liver volume increased rapidly in GAN Control and CRISPR Vehicle groups, reaching a plateau of ~3.5 cm^3 by 16-24 weeks. All three CRISPR groups increased more slowly, with CRISPR-1 and CRISPR-3 groups reaching similar levels by 32 weeks. Notably, CRISPR-2 increased a much slower rate, suggesting a mechanistic effect on the MASH-associated hepatomegaly in these animals.

9 In-vivo vs. Ex-vivo Comparison

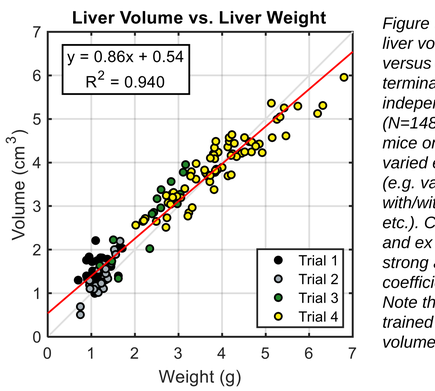

Figure 7: Comparison of in vivo liver volume measured by AI versus ex vivo liver weight at terminal timepoint of four independent mouse studies (N=148 mice). All studies utilized mice on WD and GAN diet with varied experimental conditions (e.g. variable time on diet, with/without CRISPR treatments, etc.). Correlation between in vivo and ex vivo measurements was strong as seen by high coefficient of determination (R^2). Note that the AI model was not trained on any of the imaging volumes from these studies.

10 What if AI isn't perfect?

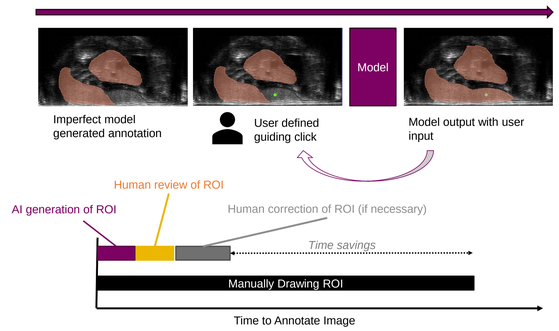

***Figure 8**: Human-in-the-loop adjustments. The models used are based on the DeepEdit architecture, which allow for user-placed guidance points. The placed points steer the model in prediction. For images where the first pass generated segmentation isn't perfect, users can still adjust the annotations with accelerated processing in iteration, generating new segmentations given previous predictions.*

11 Conclusions

In this work, we have demonstrated the feasibility of an automated AI framework for accelerating *in vivo* 3D liver volumetry in small animal MASH models requiring no human input. Using the model, we observed substantial improvement in the data analysis time with little impact on accuracy compared to the human reader.

With this technology, the practicality of performing *in vivo* volumetry and 3D image statistics at scale increases immensely, thus allowing new insights to be gained from longitudinal MASH studies.

Future work will include boosting and refining our training sets to further improve AI performance, incorporating additional animal models (e.g., liver with tumors), and making the tool available to researchers around the world to accelerate their workflow.

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