Visualization of Pancreas in Rats Using Clinical MRI and CT: from in situ to in vivo

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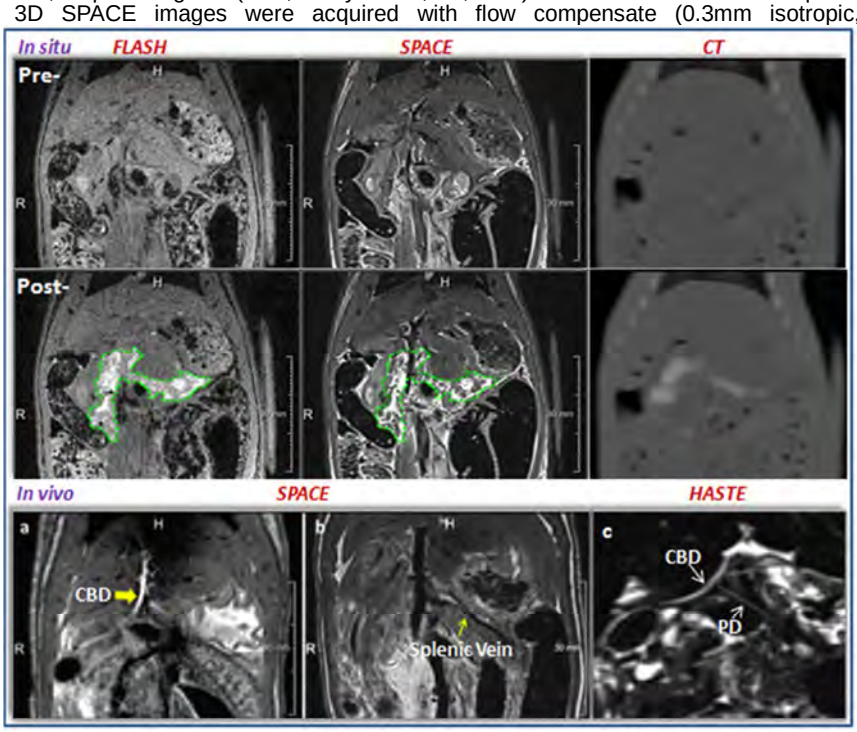
Introduction: The pancreas is an important visceral organ performing both endocrine and exocrine functions. Dysfunction of the pancreas results in diseases such as pancreatitis, diabetes, and pancreatic tumors (1,2). The high incidence and mortality of pancreatic diseases have positioned imaging diagnosis a crucial place in daily clinical practice. In order to explore the mechanisms of pancreatic pathologies and develop new diagnostic and therapeutic techniques, rodent models are often used in pancreatic studies. However, unlike pancreas in humans, which is a retroperitoneal solid organ and can be identified by imaging even without contrast enhancement (3), rodent pancreas appears as an irregular lobulated organ, which is indiscernible compared to surrounding tissues, making imaging pancreas in rodents extremely challenging (4). In this study, we intended to image rat pancreas *in situ* by using the state-of-the-art clinical MRI and CT scanners with the assistance of intra-pancreatic contrast enhancement. Detailed imaging landmarks and morphology of rat pancreas were measured, described and presented with three dimensional (3D) rendering. Meanwhile, with the help of clear recognition of rat pancreas anatomy *in situ*, attempts were made for imaging of native pancreatic landmarks *in vivo* without any contrast enhancement.

Materials and Methods: Sprague-Dawley rats about 300g were used for both *in situ* and in vivo studies. For postmortem model, the pancreas ductal secretion pathway was blocked by ligation of the biliopancreatic duct at the side close to the duodenal papilla (5). Following the baseline pre-contrasted imaging, a mixed contrast dye containing optimized concentrations of Gd-DOTA (Dotarem®, Guerbet, France, 2mM for MRI), Iomeprol (Iomeron®, Bracco, Italy, 10 mg iodine/ml for CT) and Evens blue (EB, Sigma-Aldrich, USA, for *ex vivo* coloration) was infused into the common bile duct (CBD) for postcontrast imaging. MRI was performed at a 3.0T clinical scanner (Magnetom Tim Trio, Siemens, Erlangen, Germany), combined with an 8 channel phase array wrist coil as receiver. A 0.3 mm isotropic 3D T1-weighted gradient echo (FLASH) sequence was acquired to evaluate contrast enhancement using the following parameters: TR/TE=13.74/3.69ms, FA=10 , GRAPPA=2, 1 average; corresponding T2 weighted 3D turbo spin-echo (SPACE) images were used as anatomy reference (0.3 mm isotropic, TR/TE=1500/132ms, variable FA, GRAPPA=2, 1.4 averages); Tissues with short T2 in abdomen were imaged with ultra-short echo time (UTE) sequence (0.43 mm isotropic, TR/TE=8.28/0.07ms, FA=15 , 36000 projections). CT scans were acquired using a 128-slice CT scanners (Somatom Definition Flash, Siemens, Erlangen, Germany), with a low tube voltage of 80kVp. Images were reconstructed to a matrix size of 512*512, with a slice distance of 0.2 mm. 3D high resolution MRI/CT images were post-processed with MeVisLab software package (www.mevislab.de) for MRI/CT registration, pancreatic segmentation, 3D visualization and quantification. Post-contrast MRI and CT images were registered to pre-contrast MRI space using affine transformation. Subtracted pre/post-contrast FLASH and resampled CT images were segmented using fuzzy c-mean spatial classification and region growing approach with 3D-6 nearest neighbor search. Segmentation was manually corrected by user. Meanwhile, respiration gated (SAII, Stony Brook, NY, USA) *in vivo* MRI scans were acquired while animals being anesthetized by isoflurane. 3D SPACE images were acquired with flow compensate (0.3mm isotropic, TR/TE=1500/144ms, variable FA, GRAPPA=3, 2 averages); and 2D heavy T2 weighted half-Fourier acquisition single-shot turbo spin-echo (HASTE) scans were used to assess contrast for the pancreatic duct (PD) with following parameters: 0.36*0.36*1.5mm, TR/TE=2000/250ms, FA=180 , GRAPPA=3, 6 averages.

Results: Without contrast enhancement, the pancreas was indiscernible on both MRI and CT images. After contrast infusion, only pancreatic region became outstandingly visible, as shown by CT and T1 weighted FLASH images. Hyper-intense pancreatic region outline generated from segmentation in FLASH image is delineated by green dashed line, the same outline is overlaid to SPACE image. Hyper-intense signals appeared on SPACE images indicated the presence of long T2 saline solvent. The topography of the pancreas and surrounding organs in rats was shown with 3D rendering, using re-sampled CT as bony background scaffold. The measured volume of the pancreas on MRI was 0.96±0.21 cm^3 (N=9). For *in vivo* MRI, only CBD and splenic vein could be clearly identified on 3D SPACE images as pancreatic landmarks; CBD and PD were recognized with hyperintensity on HASTE images.



Discussion and Conclusions: Due to the lack of pancreas specific labeling and unpredicted motion within the region of lower abdomen, pancreatic tissue in rodents itself is still very difficult to be distinguished from the surrounding structures, especially on 2D images. Here we presented a detailed visualization of a complete pancreas through contrast enhanced CT and MRI imaging in a rat postmortem model. The topographic landmarks created with 3D demonstration helped to provide guidelines for *in vivo* pancreatic imaging, with prominent hyper-intense signals for CBD and PD. To identify other in vivo features of rodent pancreas, contrast enhanced protocols will be evaluated in the future.

Reference: 1. Nakamura T, *et al.* 1988; 2. Cascinu S, *et al.* 2010; 3. Sainani N, *et al.* 2002; 4. Seki Y, *et al.* 2000; 5. Kara ME, *et al.* 2004.

Figure *In situ* MRI and *in vivo* MRI/CT images of rat pancreas. Common bile duct, splenic vein and pancreatic duct were indicated by arrows on in vivo MRI;
3D rendering of the pancreas (green) and surrounding organs in rats: CT bone (cinnamon), CBD (yellow), portal vein (blue), splenic vein (red), spleen (Sp, purple); stomach (St, bright grey), kidney (K, cabbage green); guts (dark grey) with ascending colon (Ac), transverse colon (Tc) and descending colon (Dc).