# Registration methodology of histology with in vivo 3T MRI for human prostate

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**Introduction:** Most of existing registration literature focuses on registering various in vivo imaging modalities including anatomical and functional MRI. Little attention has been paid to registering ex vivo histology sections. There have been efforts to register in vivo MRI with histology of rat brain scans [1]. Histology slides carry the ground truth information regarding locations and extents of tumor determined by a pathologist. With registered histology onto the in vivo MRI space, one can observe how spatial features of in vivo MRI correlate with ground truth. A methodology has been proposed for registering whole mount human prostate histology with various in vivo scans [2]. Here we refine the registration methodology and apply it to in vivo 3T diffusion MRI for two patients. We have computed the error of the registration between diffusion MRI and histology comparing tumor boundaries.

**Methods:** Registration of histology and in vivo MRI is a difficult problem as the prostate undergoes a complex set of deformation as it is removed from the body and then sectioned for histological evaluation. The registration algorithm needs to account for the complex deformations. The published methodology performs series of manageable sub-registration tasks involving intermediate modalities like specimen MRI and block face photos of the specimen instead of directly registering in vivo MRI with histology. We employ the well established mutual information (MI) based registration algorithm using thin plate spline (TPS) as the geometric interpolant for all sub-registration tasks [3]. The registration process is automatic after the initial placement of control points. The following text describes the individual sub-registration tasks. First, each histology section is registered onto the block face photo taken before the histology section was microtomed. Second, block face photos are registered onto the ex vivo specimen MRI. Finally, ex vivo specimen MRI is registered onto in vivo anatomical MRI. These sub-registration tasks can be performed more accurately since the deformations being modeled are far less complex. Each sub-registration task models different deformation thus requiring varying degrees of freedom (DOF) of the TPS, which are determined by the number and location of control points. The number and location of control points differ from one registration task to another, which can be found in Fig. 1. Block face photos are stacked to form a 3D volume before they are registered onto specimen ex vivo MRI. This stacking process further increases the information content and thus improves the accuracy and stability in registering block face photos onto specimen MRI. Additionally, in vivo diffusion MRI is registered onto in vivo anatomical MRI. In result, one can compare diffusion MRI and histology on a voxel by voxel basis in the in vivo anatomical MRI space. Previously published methodology was applied to 1.5T diffusion MRI using endorectal coil. Here we refine and apply the methodology to 3T diffusion MRI using regular body coil. Use of the regular coil instead of the endorectal coil reduces the deformation between diffusion MRI and anatomical MRI, which also uses regular coil, simpler, but there still is increased distortion with 3T diffusion MRI. We use 6 control points, two triads placed at 1/3 and 2/3 height (measured from the base of the prostate) to perform the registration.

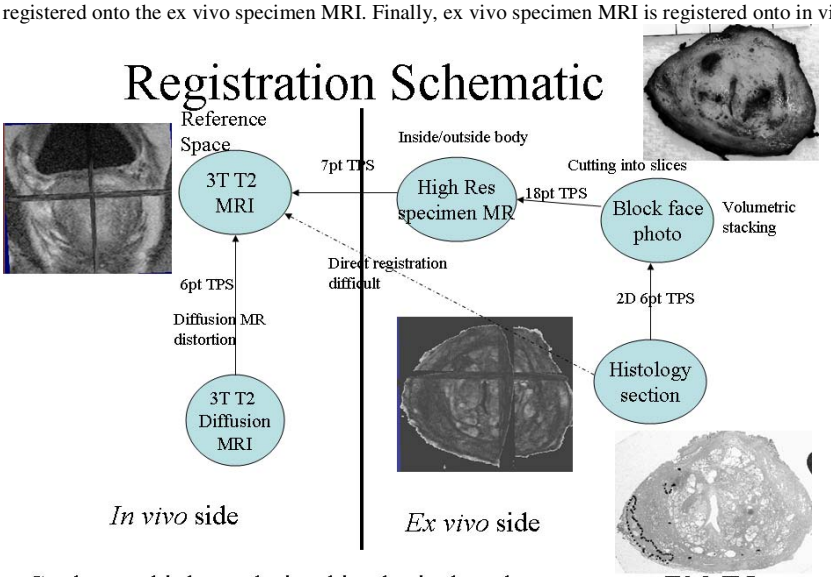


**Fig. 1.** Registration Schematic.
Solid arrows indicate each sub-registration task. Dotted arrow indicates the very difficult direct registration between anatomical MRI and histology that is improved using the sub-steps indicated by solid arrows.

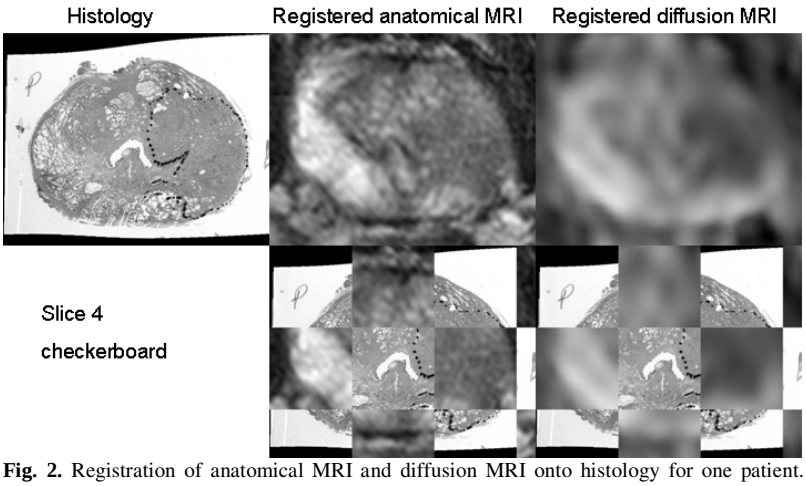


**Fig. 2.** Registration of anatomical MRI and diffusion MRI onto histology for one patient. Columns of images are histology, registered anatomical MRI, and registered diffusion MRI. Bottom row images are alternating checkerboard fusion of registered anatomical MRI and registered diffusion MRI with histology.

**Results:** Fig. 2 shows registered anatomical MRI and diffusion MRI with slice 4 of histology (out of 6 slides) for one patient. All other histology slides have been registered but not shown here. For diffusion MRI, we display apparent diffusion coefficient (ADC) images. Cancerous tissue identified with lower gray values in anatomical MRI and diffusion MRI are well aligned with tumor marking of histology. Overall registration among all three modalities is visually reasonable. We quantify the registration error by comparing tumor boundaries as locating identifiable landmarks is often difficult and unreliable. Tumor boundary in diffusion MRI can be found in low ADC area and then it is compared to the tumor boundary in the histology. Tumor boundary in anatomical MRI is unreliable. Tumor boundary in diffusion MRI may be smaller than the actual tumor extents as not all tumor cells have low ADC values. We parameterize the boundary using medial axes and compute the error as the difference between two medial axes over the range of the shorter medial axis. This way, the error measure is indifferent to erosion/dilation of boundaries but still sensitive of shape changes. The registration errors for two patients are 4.21 and 5.86 mm respectively. The resolution of diffusion MRI is 1.25x1.25x6.6 $mm^3$ or 2.18 $mm^3$ for an equivalent cubic voxel. Thus, the registration error is on the order 2 or 3 diffusion MRI voxels.

**Summary:** We have refined the existing registration methodology and applied to in vivo 3T anatomical and diffusion MRI for two cases. The registration error is computed by comparing tumor boundaries found in diffusion MRI and histology. The registration error is only 2 or 3 times the voxel dimension of diffusion MRI.

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**References:** [1] Meyer et al. J Molecular Imaging, 5:16-23, 2006. [2] Park et al. Academic Radiology, 15:1027-1039, 2008.
[3] Meyer et al. Medical Image Analysis, 3:195-206, 1997.