# **Challenges in Multimodal Image-guided Targeted Prostate Biopsy**

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# INTRODUCTION

The fusion of Magnetic Resonance Imaging (MRI) and Ultrasound (US) for targeted prostate biopsy can solve the diagnostic dilemma of patients with repeated negative prostate biopsies seen in the conventional Trans-Rectal UltraSound (TRUS) guided systematic biopsy. Recently, <sup>68</sup>Gallium labeled ligand of Prostate Specific Membrane Antigen (<sup>68</sup>Ga-PSMA) Positron Emission Tomography (PET) was introduced that, in conjunction with MRI, provides combined molecular and structural information for the detection of Prostate Cancer (PCa) [1]. Hence, we developed an open source framework [2] that combines the preoperative PET/MRI images with TRUS and provides multimodal image guidance for targeted biopsy. In this paper, we present the technical challenges in the development of multimodal image guided prostate biopsy, especially in 3D TRUS acquisition and multimodal image registration. Further, we explain the steps to address these specific challenges and some unsolved problems. Finally, we discuss the clinical evaluation of the system.

# MATERIALS AND METHODS

The multiparametric MRI and <sup>68</sup>Ga-PSMA PET were acquired on a combined PET/MR system (Siemens mMR) with 3T magnetic field strength. The 3D TRUS acquisition and biopsy were carried out in the urology department of our university hospital. We used a US system (Hitachi AVIUS) with a 2D front fire transrectal probe. However, our system is independent of the US machine as we are using a video frame grabber (StarTech) for image acquisition in HD (1280 × 1024 pixel). The US probe is tracked by an optical tracking system (NDI Polaris). We use a workstation with 2 Intel Xeon processors running at 2.13 GHz with 32GB RAM and a graphics card (Nvidia GeForce GTX Black Titan).

The clinical workflow has three steps – (i) preinterventional  $^{68}$ Ga-PSMA PET-MRI image acquisition, (ii) TRUS acquisition, 3D reconstruction and image registration, and (iii) biopsy as shown in Fig. 1. The acquisition of  $^{68}$ Ga-PSMA PET-MRI for prostate cancer imaging is explained in [1].



Fig. 1 Steps in clinical workflow.

# **3D TRUS acquisition**

The challenges in 3D TRUS acquisition are precise tracking of the 2D US probe, accurate spatial calibration of the US probe for different depth settings, and reliable 3D compounding in the standard anatomical axes.

The spatial calibration of the ultrasound probe, acquisition of tracked ultrasound, and 3D compounding are done by the fCal application available in PLUS framework [3]. We use a reference target attached to the biopsy chair, as described in [2], that facilitates the free movement of tracking camera and reorientation of the 3D TRUS volume along the standard anatomical axes.

# Multimodal image registration

The accurate modelling of the prostate deformation within clinically acceptable time limits is the main challenge for image registration and successfully targeting suspicious lesions. The review of various commercially available fusion devices is available in [4]. Most of these commercial devices use rigid image registration. The state of the art research on TRUS/MRI image registration is summarized in [5], wherein the typical approaches are either surface- or model-based. We use surface based deformable registration using Coherent Point Drift (CPD) algorithm [6] and compare it with rigid anatomical landmark based registration.

#### RESULTS

#### **Phantom studies**

For the evaluation of surface based elastic registration, we acquired MRI and TRUS images of a multimodality prostate phantom (model 053-MM, CIRS) that has visible structures such as urethra (7 mm) and three randomly placed lesions of approximately 5-10 mm. Six landmarks were annotated by an expert on images from both modalities.

The mean landmark registration errors (LRE) for surface based CPD method and rigid registration were 1.14 mm and 1.87 mm, respectively. The comparison of registration by both methods in the form of axial and coronal views is shown in Fig. 2.



**Fig. 2** Surface based elastic algorithm shows better alignment compared to rigid registration in phantom studies.

# Retrospective study on patient dataset



**Fig. 3** Surface based elastic algorithm shows better alignment compared to rigid registration in patient data.

The 3D TRUS and <sup>68</sup>Ga-PSMA PET-MRI images were acquired as per the method described earlier. The expert performed manual segmentation on MRI and TRUS images for surface extraction and annotated four pairs of anatomical landmarks in each case for the evaluation of registration.

We evaluated our registration method on five patient datasets. The mean LRE for surface based elastic registration was 2.49 mm in comparison to 4.63 mm for rigid registration. The outcome of both registration approaches for two patient cases is shown in Fig. 3.

#### **Exemplary clinical case**

After validation of the system, we used it in one multimodal image-guided biopsy. A 65 year-old patient with previous negative biopsy and rising PSA was referred for <sup>68</sup>Ga-PSMA PET-MRI examination and follow-up biopsy. In addition to the 10-core systematic biopsy, two targeted biopsy were taken from a suspicious region in the left apical zone under multimodal image guidance.

The histology confirmed significant PCa with a Gleason score of 3 + 4 = 7. The targeted biopsy cores showed the highest percentage (90%) in pathological tissue.

#### DISCUSSION

The multimodal image guidance shows a value in the detection of significant PCa, especially in men with previous negative biopsy and rising PSA. Though we tried to address some of the challenges in 3D TRUS acquisition and multimodal image registration that can be done online within short time ~5 min, some other issues in the tracking and image registration still need further work. The tracking corruption can be improved by the preprocessing of tracking stream with kalman based estimation. The image based deformation models can improve the registration in comparison with surface based methods.

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