Registration of complete 3D histological tumor datasets with in vivo MRI: first experience

F. Henning[1], R. Haase[2], S. Tokalov[1], T. Schulze[3], and N. Abolmaali[1]

[1]OncoRay - MI, Dresden, Germany, [2]OncoRay - MP, Germany, [3]Siemens Health Care Sector, Germany

Introduction

Magnetic resonance imaging (MRI) provides detailed information on morphology and its capability to display functional and metabolic information is growing steadily. Fusion of MRI with gross sectional anatomy or histology has been shown to feasible using selected slices of different specimens [1, 2]. Issues on 2D misalignment [3] and even non-rigid registration [4] have been addressed. In a clinical setting, oncologic imaging is followed by biopsy to confirm diagnosis. To the best of our knowledge, detailed registration of the entire histologic information of a tumor with in vivo MRI has not been published so far.

The purpose of our work was to fuse the entire histological dataset of a human tumor xenograft nude rat model using a clinical 1.5 T MRI scanner.

Methods and Material

MRI and tumor histology

Human non-small cell lung cancer was initiated in nude rats by subcutaneous injection of $5x10^6$ H1299 tumor cells into the hind legs one day after suppressing the immune system by whole-body irradiation with 5 Gy. After tumors reached a size of 1-1.5 cm T2-weighted imaging (voxel size: 0.2 x 0.2 x 0.2 mm³) was performed in a 1.5 T clinical MRI scanner (Avanto, Siemens) using the clinical 8-channel high-resolution knee coil. Rats were sacrificed and the tumors position in the animals was branded visible in histological staining. Tumors were excised, fixed and completely sliced in sections of 5 µm slice thickness resulting in 2000-3000 specimens. Slices were stained with hematoxiline & eosin and digitized using a microscope with a magnification factor of 1 (Fig. 1).

DICOM import of histology

We created a software application (programmed in C++ using the QT framework and the Insight Toolkit (ITK)), which is able to generate 3D image stacks in DICOM format to fuse it with MR images. The registration progress was done using a regular step gradient descent optimizer and an affine transformation. To measure misalignment quantitatively and to give the optimizer a metric to correct, the user can choose between mean square difference, Mattes' mutual information and normalized correlation. Then the generated image stack was fused with a DICOM image series manually by translating, rotating and rescaling it in three dimensions. It is possible to correct the results of registration manually. Fusion allows calculating the pixel distances in x-, y- and z- direction in physical object coordinates. With this, DICOM image series were generated. For visualization, histologic images were exported as monochrome images with modality "PET".

Results

An example of the resulting fusion of 3D MRI and 3D histology is given in Fig. 2. Fig. 3 gives a high resolution visualization of fusion with emphasis on histology.

Discussion

Registration of complete histology and MRI is possible and will reveal deeper insights into findings in MRI. The suggested technique may be applied to any MRI measurement technique, accordingly knowledge may be gathered on the reality of what we see in MRI. Main limiting factor is computer performance and the gap between the spatial resolution of histology and MRI. Application in clinical settings and for functional MRI (e.g. DWI) is suggested.

References

[1] Meyer CR et al., Mol Imaging 5: 16-23 (2006), [2] Park H et al., Acad Radiol 15: 1027-1039, [3] Malandain G et al., NeuroImage 23: 111-127 (2004), [4] Yelnik J et al., NeuroImage 34, 618-638 (2007)
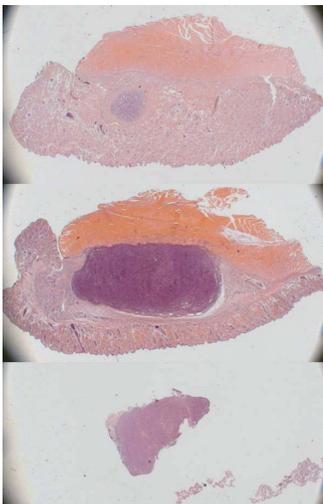
Figure 1: Three axial sections of the entire histologic work up of a subcutaneously growing human NSCLC (H1299) in a nude rat stained with hematoxiline & eosin.
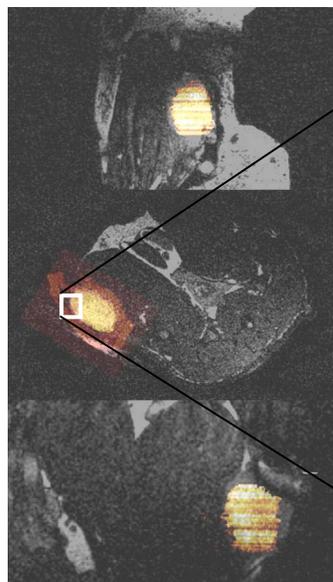
Figure 2: Fused 3D histologic and MR imaging in vivo in 3 planes.
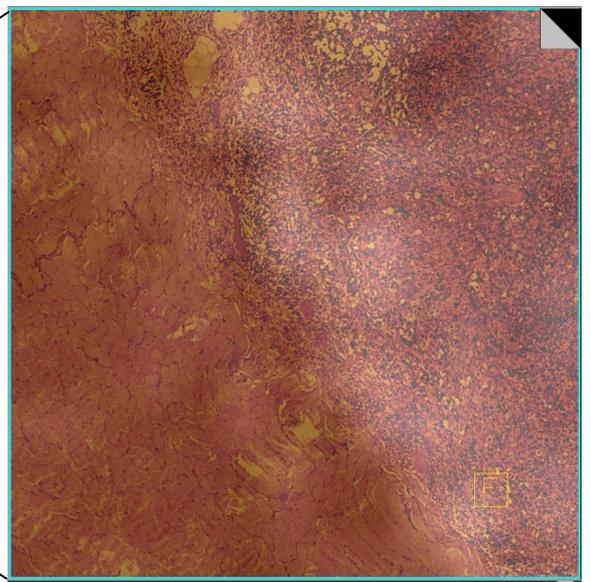
Figure 3: High resolution image fusion of in vivo MRI and histology after registration and DICOM import. Syngo is used for display.