A METHOD FOR ACCURATE SPATIAL REGISTRATION OF PET IMAGES AND HISTOPATHOLOGY SLICES

Tanuj Puri[1,], Anastasia Chalkidou[1], Arunabha Roy[1], Rhonda Henley-Smith[2], Paul R. Barber[3,4], Teresa Guerrero-Urbano[5], Richard Oakley[5], Ricard Simo[6], Jean-Pierre Jeannon[6], Mark McGurk[6], Edward Odell[2], Michael O'Doherty[1], Paul Marsden[1]*

[1]Kings College London, Imaging Sciences and Biomedical Engineering, London, UK; [2]Kings College London, Pathology Department, London, UK; [3]University of Oxford, Department of Oncology, Oxford, UK; [4]Kings College London, Institute for Mathematical and Molecular Biomedicine, London, UK; [5]Department of Clinical Oncology, Guy's & St Thomas' NHS Foundation Trust, London, UK; [6]Department of Head & Neck Surgery, Guy's & St. Thomas' Hospital NHS Trust, London, UK

INTRODUCTION

- *An accurate alignment of histopathology sections and PET images is important for radiopharmaceutical validation studies[1].*

- *We developed a method to align PET and histology images obtained in a routine pathology laboratory setting and assessed its accuracy.*

- *The method can be applied to non-parallel, non-contiguously cut and non-mega-block sized histology slices.*

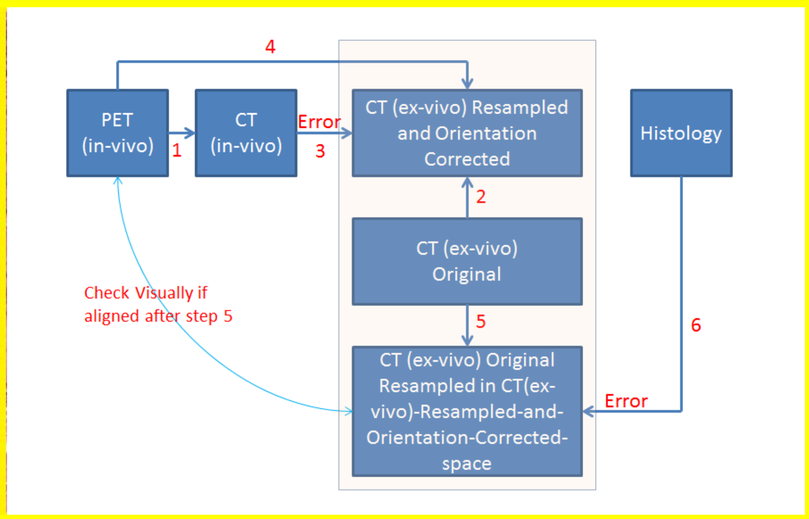

FIGURE 1 (a: Left): *A 5-micrometre (μm) thin tissue section with sea urchin spine cut orthogonally and scanned under a light microscope.* ***(b: Right):*** *The first step of the methodology is to align PET and CT (in-vivo) images with an accuracy[2] of 5.4mm using mutual information based rigid registration. In the second step, the original high resolution CT ex-vivo specimen is resampled to match CT in-vivo voxel size such that anatomical landmarks were used for in-vivo and ex-vivo CT registration. Finally, the original high resolution CT ex-vivo is orientation corrected to match the down-sampled CT ex-vivo such that the Inter-marker distances between fiducial markers were used for histology to ex-vivo CT registration. Errors were assessed using a leave-one-out strategy[3].*

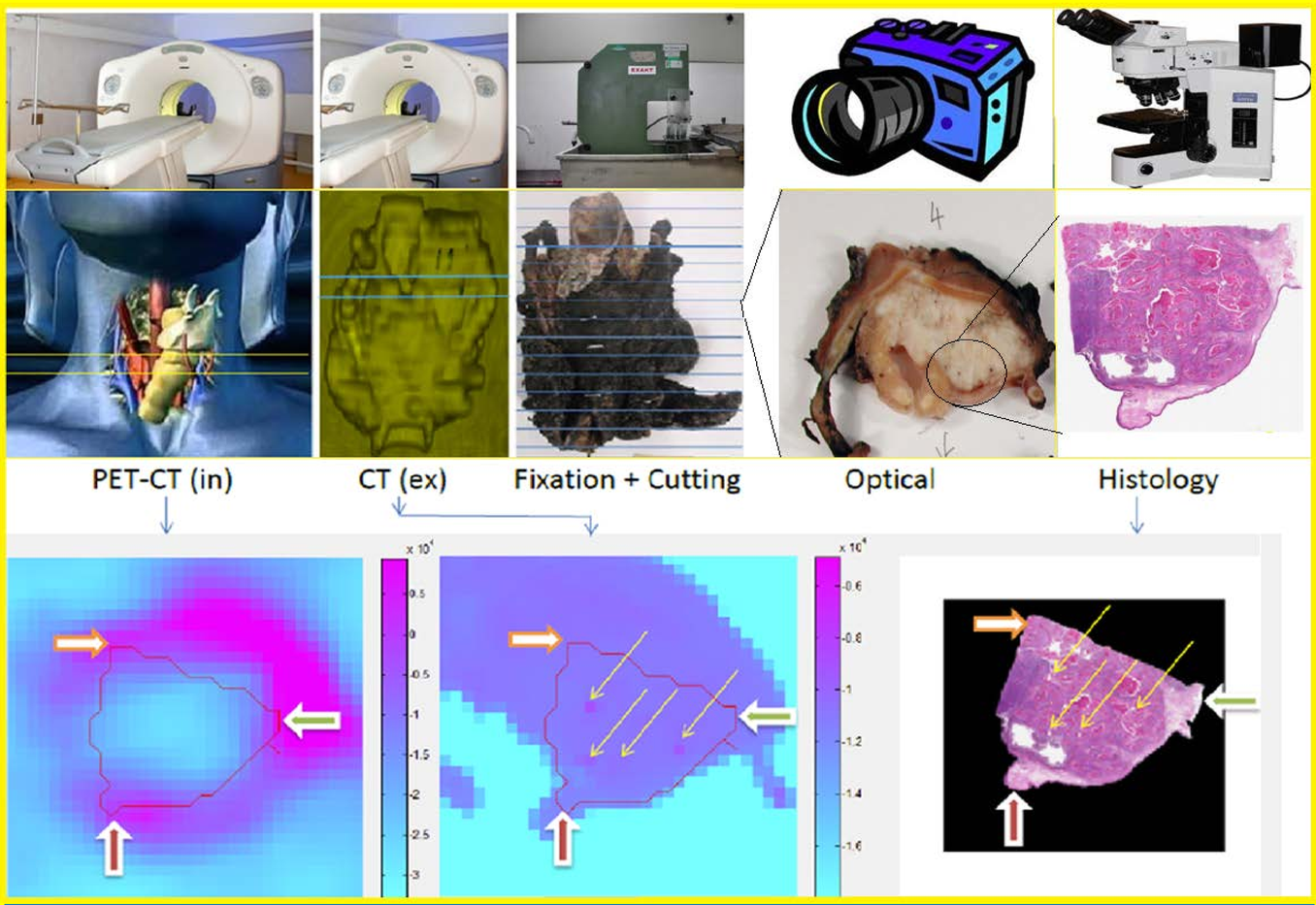

FIGURE 2: *The top row shows (from left to right) a PET scanner, CT scanner, band-saw used to slice larynx, optical camera and a light microscope. The middle row shows images of PET-CT in-vivo, CT ex-vivo, images of ex-vivo specimen fixed and sliced images taken with a camera and histology sample digitised using a light microscope. The bottom row shows registered images of PET, CT ex-vivo and histology. Regions in PET and CT ex-vivo that correspond to histology are marked with red outline. Yellow markers show the sea urchin spine markers on CT ex-vivo and histology images.*

METHODS

- *Subjects with head and neck cancer underwent a ^{64}Cu-ATSM PET-CT scan a week before surgery.*

- *After surgery, sea urchin spines (Figure 1a), which can be identified with CT, optically and histologically, were inserted into the specimen to act as fiducial markers.*

- *The specimen was fixed and scanned CT ex-vivo. After slicing, blockface images were obtained for visual reference.*

- *From these thick sectioned slices, a subsection of tissue that included tumour and markers was extracted and embedded in paraffin blocks of size 30x21 millimetre (mm).*

- *Subsequently microtome sectioning and haematoxylin and eosin staining was performed to acquire thin slides and digitised using a microscope.*

- *The methodology used to align PET and histology is described in Figure 1b.*

RESULTS

- *The PET and histology registered to CT ex-vivo are shown in Figure 2.*

- *The accuracy for registration of in-vivo to ex-vivo CTs was 2.90±0.06mm, and for registration of histology to ex-vivo CT was 1.69±0.70mm.*

- *The total registration error between PET-Histology for 10 histology samples was 6.39±0.21mm (Table 1).*

- ***The largest error in the PET-Histology registration process is due to the systematic PET-CT registration error.***

	REFERENCE	TRE-Mean(L-1-O)	TRE-Max(L-1-O)	TRE(mean)
Samples	PETin-CTin	CTin-CTex	CTex-Histology	TOTAL
1	5.40	2.83	0.91	6.16
2	5.40	2.83	1.47	6.27
3	5.40	2.83	2.58	6.62
4	5.40	2.83	1.23	6.22
5	5.40	2.94	0.93	6.22
6	5.40	2.94	2.00	6.47
7	5.40	2.94	2.96	6.82
8	5.40	2.94	1.81	6.41
9	5.40	2.94	1.04	6.24
10	5.40	2.94	1.94	6.45
MEAN	5.40	2.90	1.69	6.39
SD	0.00	0.06	0.70	0.21

TABLE 1: *The table shows (from left to right) the registration errors in millimetres for ten histology samples. TRE corresponds to target registration error. L-1-O correspond to leave-one-out. PETin corresponds to positron emission tomographic image obtained in-vivo. CTin corresponds to computed tomography image obtained in-vivo. CTex corresponds to computed tomography image obtained ex-vivo.*

CONCLUSION

We have developed a semi-automated registration method to align PET and histology images (Figure 2) with a registration accuracy of 6.39mm (Table 1) which is comparable to the PET spatial resolution.

*CORRESPONDING AUTHOR

tanujpuri82@gmail.com
tanuj.puri@kcl.ac.uk

REFERENCES

[1] Gerlinger M. et al., New Engl J Med. 366:883–892, 2012
[2] Rizzo G. et al., Q J Nucl Med Mol Imaging, 49(3):267-79, 2005
[3] Caldas-Magalhaes J. et al., Int. J. Radiation Oncology Biol Phys, 82:289-298, 2012

ACKNOWLEDGEMENTS

We would like to acknowledge King's College London and UCL Comprehensive Cancer Imaging Centre. Funded by the CRUK and EPSRC in association with the MRC and DoH (England). The authors would like to thank the staff at the head and neck bio bank, the Pathology laboratory at Guys' Hospital and PET Imaging Centre at St. Thomas' Hospital for their excellent technical support. This research is supported by the National Institute for Health Research (NIHR) Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College London. The views expressed here are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

King's College London
Cancer Imaging Centre
CANCER RESEARCH UK
EPSRC
Engineering and Physical Sciences Research Council