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

Tanuj Puri^{1,*}, Anastasia Chalkidou¹, Arunabha Roy¹, Rhonda Henley-Smith², Paul R. Barber^{3,4}, Teresa Guerrero-Urbano⁵, Richard Oakley⁵, Ricard Simo⁶, Jean-Pierre Jeannon⁶, Mark McGurk⁶, Edward Odell², Michael O'Doherty¹, Paul Marsden¹

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

METHODS

- Subjects with *head and neck cancer* underwent a ⁶⁴Cu-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 $2.90 \pm 0.06 \text{mm}$, and for registration of *histology to ex-vivo CT* was $1.69 \pm 0.70 \text{mm}$.

- The *total registration error between PET-Histology* for 10 histology samples was $6.39 \pm 0.21 \text{mm}$ (Table 1).

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

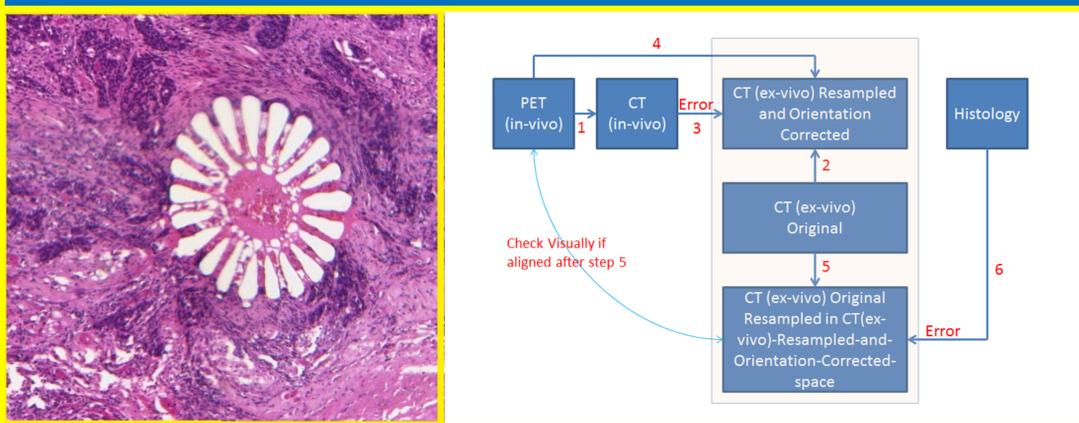


FIGURE 1 (a: Left): A 5-micrometre (μm) thin tissue section with *sea urchin spine* cut orthogonally and scanned under a light microscope. **(b: Right):** The first step of the methodology is to align PET and CT (in-vivo) images with an accuracy² of 5.4mm using *mutual information based rigid registration*. 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.

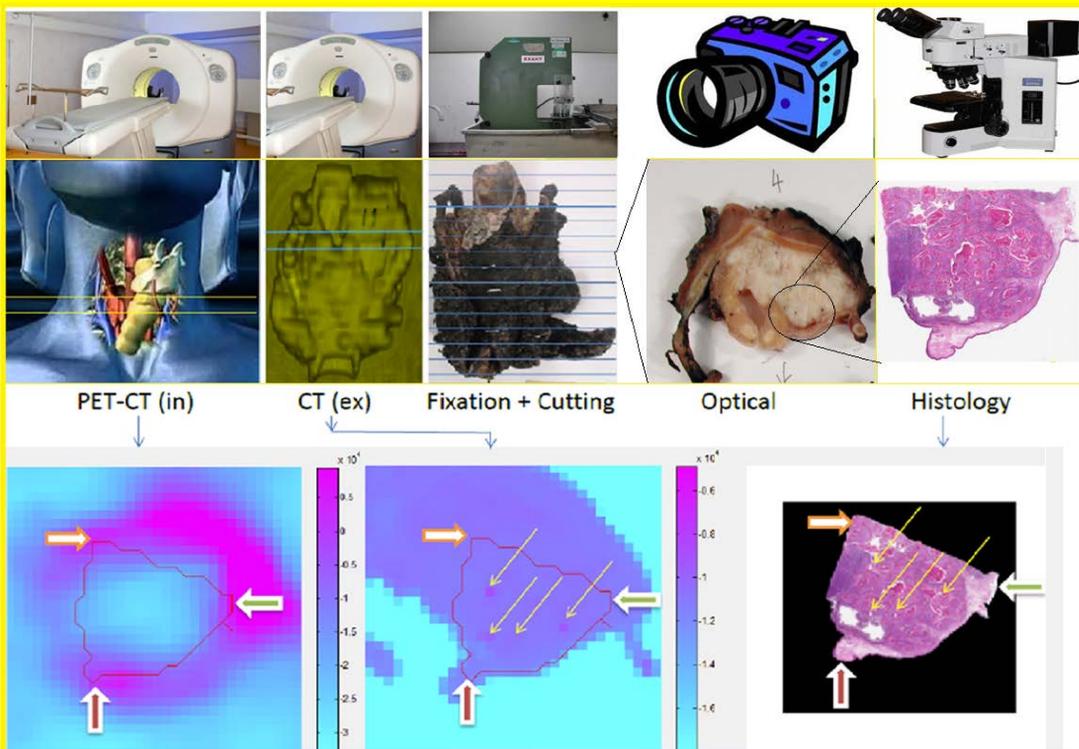


FIGURE 2: The top row shows (from left to right) a PET scanner, CT scanner, band-saw used to slice larynx, optical camera and a light microscope. The middle row shows images of PET-CT in-vivo, CT ex-vivo, images of ex-vivo specimen fixed and sliced images taken with a camera and histology sample digitised 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*.

	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

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