PhD Thesis title: 'Uncertainties in prostate targeting during radiotherapy: assessment, implications and applications of statistical methods of process control**'**

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ABSTRACT:
In the last 15 years, a great deal of effort has been expended on developing and investigating various aspects of image-guided radiotherapy (IGRT). IGRT of the prostate gland is of particular interest due to the highly mobile nature of the organ and its proximity to radiosensitive organs. This thesis sets out to quantify some uncertainties that may impact IGRT processes for the specific case of prostate targeting using fiducial markers. Methods inspired by Statistical Process Control (SPC) for improving existing techniques and setup correction strategies in IGRT of the prostate are also demonstrated.
A number of uncertainties that may affect the accuracy of fiducial tracking using an electronic portal imaging device (EPID) were investigated. The impact of beam-collimation device errors, inter- and intra-observer variability, and the subtended angles for stereoscopic registration using the radiation field-edge detection method were firstly quantified experimentally via a phantom study. This study was extended to evaluate the impact of errors of the beam-collimation device on treatment plans for intensity-modulated radiotherapy (IMRT) of the prostate. Results showed that errors in beam-collimation devices affect the accuracy of localization measurements as well as the dose distribution of IMRT plans for prostate treatment. However, assuming good practices in machine quality assurance are applied, the clinical impacts of these geometric collimation errors are dwarfed by the potential magnitude of the patient-related displacment of the prostate.
The above study was followed by an investigation of the uncertainty of tracking and registering fiducial markers. It was demonstrated that this type of uncertainty is related to potential changes in the IGRT process, which may compromise the quality of radiation treatment delivery. In selected cases, this uncertainty was shown to be related to the presence of unusually large rotational displacements and uniform shrinkage of the prostate during radiotherapy.
The use of EPID for tracking fiducial markers to correct patient setup is well established. However, EPID images do not provide information about soft tissue. A dose-reduced imaging protocol using kilovoltage cone-beam computed tomography (kV-CBCT) and fiducial markers was proposed to overcome this limitation. The scan angle for this protocol is 200^{o} and so scans deliver a relatively low imaging dose, typically 3.7 mGy per fraction, or 0.2% of the typical treatment delivery dose per fraction. The comprehensive comparison study in this thesis demonstrated that low-

dose CBCT is equivalent to the present standard of care in IGRT for localization using fiducial markers.

This thesis has also explored the use of SPC methods for two applications in IGRT of the prostate. Firstly, the SPC method was used to track uncertainties in point-based rigid-body stereoscopic registration over time. The Fiducial Registration Error (FRE) was used as a quantitative metric to represent residual errors in registration. The SPC method using an *x*-chart was shown to correctly indentify individual cases with significant and/or systematic changes in FRE over time, indicating that rigid-body registration may not remain valid at all points throughout a course of treatment. Secondly, the concept of SPC was applied to the adaptation of treatment based on changes in the localization components within a correction strategy with a non-zero action level. The cumulative-sum (CUSUM) method in SPC was demonstrated to be feasible for the identification and correction of systematic changes in the localization offsets across a wide range of non-zero thresholds that may be used in a clinical setting. The applications of SPC methods described above were demonstrated through retrospective studies using IGRT data acquired from real patients.

References to author publications that relate specifically to the dissertation:

Ung NM, Harper C and Wee L (2011) "Dosimetric impact of systematic MLC positional errors on step and shoot IMRT for prostate cancer: a planning study." *Australas. Phys. Eng. Sci. Med.* 34(2): 291-8.

Ung NM and Wee L (2011) "Fiducial registration error as a statistical process control metric in image-guidance radiotherapy with fiducial markers." *Phys. Med. Biol.* 56(23): 7473-85.

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Ung NM and Wee L (2012). “On the accuracy of localization achievable in fiducial-based stereoscopic image registration system using electronic portal imaging device.” *Australas. Phys. Eng. Sci. Med.* 35(2): 205-13.