On-line image-guided HDR brachytherapy (IGBT) for prostate cancer using ultrasound based real-time solution

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Abstract. A new solution exists for prostate HDR brachytherapy, allowing seamless real-time procedure based on ultrasound imaging, compared a conventional approach with separate sessions for catheter insertion, CT imaging, planning and verification before treatment. This introduces a new paradigm into HDR brachytherapy procedure – no requirement for patient transfer while enabling real-time image guidance throughout the procedure including ‘beam-on’ time. In this work a seamless integration of real-time workflow has been designed, which demonstrates the efficacy of ‘plan and treat’ solution, in particular, with minimising geometric miss via a new on-line image guidance protocol.

1. Introduction
HDR brachytherapy (HDR-BT) is a mature treatment modality to precisely deliver hypofractionated radiation dose for various sites including prostate, skin, sarcoma, breast and gynaecologic cancer [1, 2]. Conformity of dose distribution is inherently superior to external beam radiotherapy (EBRT) allowing reduced toxicity for organs-at-risk adjacent to (even inside) the target. HDR-BT is particularly useful to ‘boost’ dose to target (e.g. prostate), combined with relatively homogeneous dose distribution administered by EBRT [3]. However, it is inevitable for conventional off-line CT-based HDR-BT to involve separate sessions with catheter insertion, simulation, planning and treatment verification, which are labour-intensive in terms of theatre scheduling as well as multidisciplinary team staffing. In addition, it is necessary to transfer patients multiple occasions throughout their treatment, which can limit dosimetric and geometric accuracy of treatment delivery, directly relating to undesirable local control and toxicity [4, 5].

Ultrasound (US) imaging system is portable and it can provide an excellent visibility of the prostate and its surrounding anatomy [5]. This fact consequently led to the developments of US-based intraoperative HDR-BT. A modern brachytherapy treatment planning system (TPS), e.g. Oncentra Prostate™ (Nucletron B.B., Veenendaal, The Netherlands), combines transrectal ultrasound (TRUS) imaging and its volumetric reconstruction techniques with conventional TPS functions such as 3D catheter reconstruction, dose calculation, optimisation and its evaluation. This solution uses the ultrasound (US) echoes of the implant needles for the definition of the needle position on two orthogonal live images, enabling TRUS image-guided ‘plan and treat’ procedure for prostate HDR-BT. This allows a real-time adaptive approach for any changes of anatomy at any time of the procedure. Oncentra Prostate™ has been recently implemented in Peter MacCallum Cancer Centre (PMCC) in order to administer more effective and efficient treatment procedures, compared to the
existing CT-based HDR solution Oncentra™ Brachy (Nucletron B.B., Veenendaal, The Netherlands). This work focuses on the clinical implementation of this new technique, including on-line HDR image-guided brachytherapy (HDR-IGBT) workflow.

2. Materials and Methods
A series of commissioning tests has been performed to implement Oncentra Prostate™ for ultrasound imaging, catheter reconstruction, dose calculation and optimisation as well as independent dose calculation system. US volumetric reconstruction and live catheter reconstruction accuracy were characterised for ProGuide (round plastic) needle and Trocar (sharp stainless steel) needles using methods described in Siebert et al.’s work [6]. Ten different depths were measured by two different observers (i.e. n = 20). An optimisation algorithm (HIPO) in Oncentra Prostate™ was compared to the existing algorithm (IPSA) in the Oncentra™ Brachy. A seamless integration of real-time workflow has been designed and demonstrated. Tolerance for online image-guidance results were set based on 20 consecutive treatment fractions.

3. Results
Motorised ultrasound 3D-imaging could accurately reconstruct volumetric images within the uncertainty defined by slice thickness. This could be confirmed by scanning both transverse and longitudinal direction with turning ‘grid-on’ in ultrasound unit, where the US grid was used as a digital grid phantom given the fact that grid dots are exactly equidistant (5mm) and its connected lines are perfectly parallel or orthogonal to each other – its example is depicted in Figure 2. This simple procedure could effectively detect volumetric reconstruction error within slice thickness; hence, this has been incorporated into daily QA before the real-time HDR-BT procedure. US image with modified setup provides good image contrast for target region as well as organs-at-risk with no radiation dose.

A ‘virtual catheter’ can guide catheter insertion and real-time correction of catheter reconstruction is possible based on live image. Catheter reconstruction could be accurately performed for both round plastic (ProGuide) and sharp stainless steel (Trocar) needles, based on ultrasound image within 1 mm (0.5±0.4 mm) measurable uncertainty (average error ± 2SD from 20 measurements). The trocar needle has a sharper tip providing better catheter tip definition while inherently more ultrasound artefact due to its high-Z component, compared to the round plastics; hence, both types of needle show equivalent catheter reconstruction accuracy.

Table 1 shows dosimetric comparison between CT-based planning with IPSA and US-based real-time planning with HIPO for 40 consecutive fractions treated in PMCC (20 patients from each technique). Compared to the former technique, the newer technique showed reduction of V150% and V200% of the target volume by 24% and 13%, respectively, while D30% and D10% of urethra are kept within 5% change, which is still far less than tolerance dose. This implies more homogeneous dose distribution for efficient planning (i.e. DVH optimisation) with an appropriate set of user input (e.g. plan objective and constraints), which agree with a previous study [7].

![Figure 1. An example of 3D view of volumetric US image – its scan performed with US grid-on as a digital phantom to assess volumetric image reconstruction, showing negligible reconstruction error within slice thickness (0.5mm).](image-url)
Table 1. Comparison of DVH parameters for target (prostate plus margin) as well as urethra between CT-based planning with IPSA and US-based real-time planning with HIPO.

| Parameter       | CT-based planning with IPSA | US-based real-time planning with HIPO |
|-----------------|----------------------------|--------------------------------------|
| $V_{\text{target}}$ (in cc) | 37.3 (± 9.8) cc             | 36.8 (± 9.9) cc                      |
| $V_{150\%}$ (CTV)           | 31.9 (± 3.1) %              | 24.3 (± 2.4) %                       |
| $V_{200\%}$ (CTV)           | 12.6 (± 2.3) %              | 7.9 (± 1.0) %                        |
| $D_{50\%}$ (Urethra)        | 98.6 (± 3.1) %              | 104.8 (± 2.2) %                      |
| $D_{10\%}$ (Urethra)        | 103.1 (± 3.2) %             | 109.3 (± 2.8) %                      |

Figure 1. An example of 3D view of volumetric US image – its scan performed with US grid-on as a digital phantom to assess volumetric image reconstruction, showing negligible reconstruction error within slice thickness (0.5mm).

Figure 2. Three snapshots of 4D-movie file during treatment with noticeable rectal movement, causing anatomy change during beam-on. Two dashed lines and three arrows overlaid (yellow) on the images: the lower to indicate rectal movement in a) compared to the other images, and the upper to indicate live catheter shift posteriorly in c) compared to the other images c). Three yellow arrows in each of the three snapshots highlight undesired over-dosage to rectum (i.e. closer to radiation source than what is planned).

Figure. shows three snapshots of live US cine 2D-imaging during treatment, illustrating an incidence of gating events due to noticeable rectal movement, which caused entire anatomy change in the imaging field-of-view during beam-on. Two dashed lines and three arrows overlaid (yellow) on the images: the lower line to indicate rectal movement in a) and b) compared to c), and the upper to indicate live catheter shift posteriorly in c) compared to the other images. Three yellow arrows in each of the three snapshots show undesired over-dosage to rectum (i.e. closer to radiation source than what is planned). This result clearly demonstrates that 2D-live ultrasound cine image during treatment can ensure accurate treatment delivery. Based on 20 consecutive patients’ treatments, action level for beam-off and thereafter immediate adaptation has been set as 3 mm for longer than 5 seconds for displacements of urethra and rectum from the planned positions, where rectum movement is only considered anteriorly towards catheters. In addition, post-treatment image acquisition and 3D reconstruction with overlaying the treated plan and structure could verify any possible deviation in patient geometry before and after the procedure dose, as like post-treatment CBCT in external beam radiotherapy, yet with nor cost neither radiation dose. This retrospective study could pick up changes between planned and actually delivered in terms of dosimetry, therefore it can possibly correlate undesired over-dosage to OARs with its consequent toxicity (if there are any).

4. Discussion
In conventional off-line CT-based HDR-BT, there is little (or no) contrast between prostate target and surrounding tissue, hence CTV contouring and PTV margin tends to be conservative [4, 5]. In contrast, US image-guided intraoperative HDR-BT provides excellent contrast between prostate and surrounding organs-at-risk, hence it seamlessly integrates all of separate sessions in the conventional technique, enabling real-time workflow. There are several advantages in the new technique; first of all, this single non-stop procedure can minimise patient movement and implant shift. If there are any
changes, the new technique enables on-line adaptive HDR-BT to account for geometric changes of anatomy as well as sub-optimal catheter placement at any time point throughout the procedure. In addition, this solution provides virtual planning option to visualise what patients will get before catheter insertion, which will be particularly useful for less experienced brachytherapy team. Most importantly, US-based real-time HDR-BT enables on-line image-guided treatment option to monitor anatomy changes and to actively act on it by ‘beam-off’ (gating). It can be argued that prostate moves together with catheters (radiation source), hence, there is no change in target coverage; however, distance from the catheters to OARs (e.g. rectum, urethra or bladder) can be changed – reduction in the distance is detrimental, therefore there can be undesirable over-dosage to surrounding tissues.

On the other hand, US-based real-time technique has its own limitations. The procedure requires at least two image acquisitions before and after catheter insertion. Accurate implant placement, planning and treatment are based on an assumption that the two images share a same image coordinate origin, (i.e. identical TRUS probe position relative to anatomy between the two images), which is represented by a transverse transducer of TRUS probe at a base-plane of prostate. It is a non-trivial to validate this assumption due to two reasons: i) anatomy changes after catheter insertion – prostate is pushed in superiorly and stretched as well as swollen, and ii) US image after implant is subject to time-of-flight artefact, caused by heterogeneity from the catheters. Hence, the two images before and after implant always look different. In addition, there are also similar artefacts at the tip of catheters, which is crucial to accurately reconstruct catheters. Catheter reconstruction accuracy is deemed equivalent between Proguide (plastic) needle and Strocar (stainless steel) needle. Both cases, uncertainty due to US artefact is up to 1mm, which results agree with other study [6]. These two factors can cause discrepancies in free-length (catheter length out-of-template) between actual measurements and what TPS thinks which can be detrimental to clinical outcome. Hence, it is highly recommended to ‘remember’ anatomy at the base-plane by capturing its image before image acquisition without implant. Furthermore, target contouring is difficult in the image after implant due to similar US artefacts. Hence, it is important to contour on the image before implant then correlate catheter position to the contoured target, in order to minimise difference in actual anatomy and how its planned. It is undoubtable that brachytherapy team needs an expert trained for US image and its system, which is often not a usual case in routine clinical practice. All of the aforementioned limitations need to be carefully addressed to maximally enhance advantages of this new technique.

The authors consider US live image as an invaluable tool to enable on-line image-guided HDR-BT. 2D-live image plays an important role as ‘a safety belt’ during treatment. There were two gating events over last 12 months according to our on-line image guidance protocol shown in the result section – one for rectal movement and the other for patient-coughing induced anatomy shift causing reduced distance from catheter to rectum as well as urethra rotation. Such cases would be detrimental in the conventional procedure without on-line image guidance. The US imaging system also offers additional advantage of post-treatment image and its 3D reconstruction (like post-treatment CBCT in EBRT) – this is to further confirm how much changes are involved before and after treatment, so as to retrospectively quantify potential difference between what is planned and treated.

It is worth noting that real-time ‘plan-and-treat’ procedure is deemed less time-consuming, hence more efficient compared to the CT-based conventional procedure. At the same this can be more effective with improving quality of plan and its delivery. According to our experience, after the first three-month learning curve with the new technique, 0.45 day per fraction is achievable with the same number of staff as opposed to 0.65 day per fraction for the conventional technique. In other words, 30% less staff are needed per given time to treat a same number of patients.

5. Conclusion
Ultrasound-guided real-time HDR-BT solution enables a single non-stop adaptive procedure within an operation room, minimising patient movement and implant shift [8]. More importantly, on-line IGBT could be effectively implemented for real-time treatment delivery verification and estimate the dose delivery to the insertion position with zero geometric uncertainty. There are some limitations including
image artefacts and reproducibility of finding a same base-plane before and after catheter insertion, which need to be addressed. It is worth noting that total procedure time could be significantly reduced without compromising the quality of treatment procedure, aiming for 3-4 hours per procedure.

6. References
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