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### Paper:

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1 Automated algorithm for CBCT-based dose  
2 calculations of prostate radiotherapy with  
3 bilateral hip prostheses  
4

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39 **Objective:** Cone beam CT (CBCT) images contain more scatter than a conventional CT  
40 image and therefore provide inaccurate Hounsfield units (HU). Consequently CBCT  
41 images cannot be used directly for radiotherapy dose calculation. The aim of this study is  
42 to enable dose calculations to be performed with the use of cone-beam CT images taken  
43 during radiotherapy and evaluate the necessity of re-planning.

44 **Methodology:** A prostate cancer patient with bilateral metallic prosthetic hip replacements  
45 was imaged using both CT and CBCT. The multilevel threshold algorithm (MLT) was used  
46 to categorise pixel values in the CBCT images into segments of homogeneous HU. The  
47 variation in HU with position in the CBCT images was taken into consideration. This  
48 segmentation method relies upon the operator dividing the CBCT data into a set of volumes  
49 where the variation in the relationship between pixel values and HUs is small. An  
50 automated MLT algorithm was developed to reduce the operator time associated with the  
51 process. An intensity modulated radiation therapy (IMRT) plan was generated from CT  
52 images of the patient. The plan was then copied to the segmented CBCT data sets with  
53 identical settings and the doses were recalculated and compared.

54 **Results:** Gamma evaluation showed that the percentage of points in rectum with  $\gamma < 1$   
55 (3%/3 mm) were 98.7% and 97.7% in the segmented CBCT using MLT and the automated  
56 MLT algorithms, respectively. Compared with the planning CT (pCT) plan, the MLT  
57 algorithm showed -0.46% dose difference with 8 hours operator time while the automated  
58 MLT algorithm showed -1.3%, which are both considered to be clinically acceptable, when  
59 using collapsed cone (CC) algorithm.

60 **Conclusion:** The segmentation of CBCT images using the method in this study can be used

61 for dose calculation. For a prostate patient with bilateral hip prostheses and the associated  
62 issues with CT imaging, the MLT algorithms achieved a sufficient dose calculation  
63 accuracy that is clinically acceptable. The automated MLT algorithm reduced the operator  
64 time associated with implementing the MLT algorithm to achieve clinically acceptable  
65 accuracy. This saved time makes the automated MLT algorithm superior and easier to  
66 implement in the clinical setting.

67 **Advance in knowledge:** The MLT algorithm has been extended to the complex example  
68 of a patient with bilateral hip prostheses, which with the introduction of automation is  
69 feasible for use in ART, as an alternative to obtaining a new planning CT and re-  
70 outlining the structures.

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## 84        **1        Introduction**

85        One of the desirable objectives during external beam radiotherapy (EBRT) of the prostate  
86        is the delivery of an uniform radiation dose to the treatment volume while sparing organs  
87        at risk. In practice, this may be difficult to achieve due to day-to-day changes in patient  
88        positioning, patient shape and internal organ movement during the treatment course (1).  
89        Interfractional motions such as variations in bladder and rectum volume have been  
90        demonstrated to have significant effects on prostate position and a negative impact on the  
91        accuracy of the treatment course (2).

92        The implementation of image guided radiation therapy (IGRT) in clinical practice, such  
93        as kilovoltage cone beam computed tomography (kV-CBCT), has improved tumor  
94        targeting and tumour control during the treatment delivery process and reducing dose  
95        delivery to normal tissues. CBCT has been used to correct patient set-up in the treatment  
96        position and to monitor any anatomical deformations in 3D with sufficient soft tissue  
97        contrast (3). In addition, CBCT can be feasible for adaptive radiotherapy (ART), e.g. dose  
98        recalculation, if the Hounsfield units (HU) are accurate and reliable (4).

99        Due to its cone-beam geometry, the amount of scatter in CBCT images is greater than  
100        that of conventional CT images (fan beam), and is dependent on the scanned object size,  
101        the collimator and the filter used (5). The image quality also depends on acquisition  
102        parameters, i.e. mA, kV and the number of projections. In addition, limited gantry rotation  
103        speed and large field-of-view (FOV) in a single rotation reduce image quality. Therefore,  
104        CBCT images provide inaccurate HUs and, consequently, cannot be used directly for dose  
105        calculation (6). Therefore, if there are significant anatomical changes observed on the

106 CBCT images, acquiring another CT is necessary for an accurate assessment of dose  
107 differences. This procedure is time consuming across all staff groups involved in the  
108 radiotherapy pathway and additional dose is delivered to the patients. Thus it would be  
109 sufficient to use CBCT images that were already taken during radiotherapy for evaluating  
110 the necessity of re-planning. Many papers have studied the use of CBCT data for dose  
111 recalculation, which is still an active area for research (6).

112 To deal with HU calibration of CBCT images, Richter et al (2008) proposed a method  
113 where HU-electron density conversion curves were based on average CBCT HU values for  
114 separate treatment sites in order to generate population-specific conversion curves (7).  
115 Such an approach is still subject to CBCT artefacts and can result in dose calculation errors  
116 of greater than 5% when compared to planning CT (pCT) -based dose calculation (6). Some  
117 studies deal with correcting scatter by applying quite unsophisticated software corrections  
118 to CBCT images before reconstruction (8). Such a method may be unable to accurately  
119 reconstruct higher-density material for a large scanned object size. In addition, it may be  
120 difficult to implement such a method in a clinic even though recent commercial software  
121 releases provide sophisticated scatter correction algorithms (9).

122 Other studies deal with adjustment techniques to correct CBCT HU values, such as  
123 mapping the HUs in CT images to the equivalent points in the CBCT image geometry after  
124 rigid or deformable image registration (10, 11). In addition, image cumulative histograms  
125 can be used to adjust HU values between pCT and CBCT images (10, 14). Another  
126 technique uses a multilevel threshold (MLT) algorithm as proposed by Boggula et al  
127 (2007), where the pixel values of CBCT images were replaced with a small number of fixed  
128 HU values as in CT for air, soft tissue and bone (12-14). Onozato et al (2014) excluded

129 water and used fat and muscle instead, resulting in a dosimetric difference below 2% (14).  
130 In addition, Fotina et al (2008) used the same technique, calling it a density override  
131 technique, but with a range of HU values for bone (soft bony structures, hard bone and  
132 teeth) and air/low density regions (rectal balloon and lung). All other regions are assumed  
133 to be water-equivalent assigned with one HU value, resulting in a dosimetric difference  
134 below 2% (6).

135 Recently, Dunlop et al (2015) assessed the CBCT dose calculation accuracy for density  
136 override approaches for four pelvis cases, where CBCT voxels were assigned as water only  
137 and then as either water or bone (water only and water-and-bone methods). This was then  
138 compared with a scatter correction and automated density override approach that is  
139 available in the RayStation TPS (V3.99, RaySearch Laboratories, Stockholm, Sweden) (9).  
140 In the automated density override approach, six different densities (air, lung, adipose tissue,  
141 connective tissue, cartilage/bone, and higher density for prosthesis) are assigned to the  
142 CBCT image by binning the CBCT image histogram into six density levels. Compared  
143 with pCT acquired on the same day as the CBCT, the results showed that the automated  
144 approach was superior to the other methods, when considering smaller patients (with  
145 anterior-posterior distance < 25 cm). For larger patients, the water only method gave the  
146 best accuracy.

147 The occurrence of inhomogeneities in the patient anatomy, e.g. hip replacements, has the  
148 ability to complicate the automated process, requiring the addition of additional set  
149 densities. In fact, none of the above studies used a patient with prostheses, which would  
150 provide a more general assessment of dose calculation using CBCT. Almatani et al (2016)  
151 studied CBCT-based dose calculations of a prostate patient with a single hip prosthesis

152 using the MLT algorithm. The work showed that it was necessary to extend the MLT  
153 algorithm to categorise pixel values into segments on a region-by-region basis, with the  
154 region size changing depending on the anatomical features (15). In addition, a larger  
155 number of materials (up to 8) than typically used in previous works was explored. The  
156 results showed that five values of HU (air, adipose, water, cartilage/bone and metal  
157 implant) gave the best balance between dose accuracy ( $-1.9\%$ ) and operator time (3.5  
158 hours). However, the length of operator time needed could make it difficult to implement  
159 this as a technique in the clinic.

160 The aim of this work is to develop a more robust method to account for the full range of  
161 patient size as well as the difficulties presented by the metal artefacts in both pCT and  
162 CBCT images. A CBCT-based dose calculation of a patient with bilateral metal hip  
163 prostheses is presented using the extended MLT algorithm, in the same manner extending  
164 upon proposed previously by the authors for a single hip prosthesis. In addition, an  
165 automated MLT algorithm was developed to reduce the operator time associated with the  
166 manual MLT algorithm. With the flexibility of a region-by-region approach, it is envisaged  
167 that the method can be applicable for the automation of dose calculation on segmented  
168 magnetic resonance (MR) images and could be of interest to MR-based ART (9).

## 169 **2 Method and materials**

### 170 **2.1 CBCT image acquisition**

171 The X-ray volumetric imaging integrated in an Elekta Synergy linear accelerator (XVI<sup>TM</sup>,  
172 version 4.5, Elekta, Crawley, West Sussex, UK) was used to acquire CBCT images. The  
173 CBCT scans were acquired with a field of view (medium FOV) of 41 cm in diameter and



174 17.85 cm in the axial direction with a bowtie filter added (F1). CBCT images were  
175 reconstructed with 1 mm cubic voxels and averaged in the longitudinal direction for 3 mm  
176 slice thickness. The images were then transferred to the Oncentra MasterPlan (OMP)  
177 treatment planning system (version 4.3 Elekta, Netherlands) via DICOM protocol for dose  
178 calculation.

## 179 **2.2 Patient study**

180 This study was performed on a patient with bilateral metal hip prostheses replacement  
181 treated at the Department of Clinical Oncology and Radiotherapy, South West Wales  
182 Cancer Centre ABM University Health Board, Swansea, Wales. The anterior-posterior  
183 (AP) separation of the patient was 26.5 cm. Such a challenging case provides a good  
184 assessment of dose calculation using CBCT due to the difficulties presented by the metals  
185 artefacts in both pCT and CBCT images. The artefacts in pCT were reassigned as water in  
186 the original patient plan using a bulk density correction (Fig. 1a). An intensity modulated  
187 radiotherapy (IMRT) treatment with five 6-MV photon fields, at gantry angles of 35°, 145°,  
188 180°, 235°, and 300° was performed. The prescription dose was 70 Gy in 35 fractions.  
189 Dose distribution was calculated using pencil beam (PB) and collapsed cone (CC)  
190 algorithms to allow the comparison with Monte Carlo (MC) algorithm and to identify the  
191 effects of HU on dose calculation.

## 192 **2.3 Modification of CBCT images**

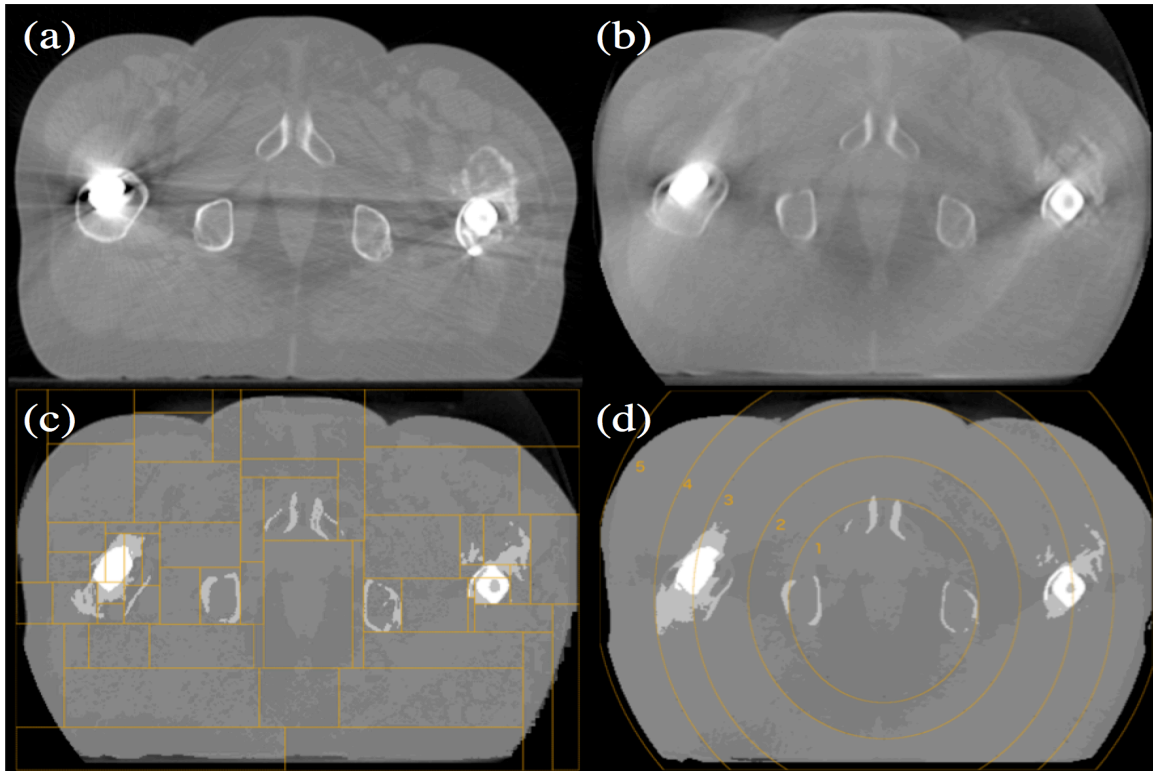
193 The MLT algorithm, used to correct CBCT data, involves categorising pixel values in the  
194 CBCT images into segments of homogeneous HU using MATLAB scripts (Mathworks,

195 Natick, MA) to generate segmented CBCT (sCBCT) data. Based on Almatani et al (2016),  
196 the binning of CBCT images of a patient with hip prosthesis into five HU values results in  
197 sufficiently accurate and clinically acceptable dose distribution (15). Considering more  
198 than five HU values provides more anatomical information and improves dose calculation  
199 accuracy (by 0.23%) but would require more operator time (58%), as the sensitivity  
200 increases when increasing the number of HU bins to define the material type. Therefore, in  
201 this study, five values of HU values were used to segment CBCT images that represent, air  
202 (-976 HU), adipose tissue (- 96 HU), water (0 HU), 2/3 cartilage & 1/3 bone (528 HU)  
203 and metal implants (2976 HU). The ranges of pixel values in the CBCT images were: air  
204 (0 to 200), adipose tissue (201 to 700), water (701 to 875), 2/3 cartilage & 1/3 bone (876  
205 to 1600) and metal implant (1601 to 8000).

206 The threshold values for each material at these intervals are dependent on the geometry  
207 since noise and scatter in CBCT is variable, especially in the presence of high density  
208 materials, as shown in Figure 1(b) (16). In this study, the MLT algorithm was used in two  
209 ways, using a manual and an automated procedure. In the manual procedure, the CBCT  
210 images were divided into regions with sets of different threshold values, which are  
211 determined on a region-by-region basis, to sufficiently correct for the artefacts. The shape  
212 of each region is a rectangular cuboid. In general, the greater the variation in the scatter,  
213 the greater the number of regions that need to be considered, and the size of the region  
214 decreases as it gets closer to inhomogeneities. The resultant segmented CBCT images using  
215 this procedure are referred to as sCBCT<sub>man</sub>.

216 In the automated procedure, the CBCT images were divided into five concentric rings,  
217 which are uniform in shape through all slices, using MATLAB scripts, as shown in Figure  
218 1(d). The centre of the inner radius (radius 1) was defined at the centre of the patient  
219 geometry, which can be changed by the user. The lower threshold values for each material  
220 changes with the radius but is easily determined by the user's analysis of the central slice.  
221 For example, the lower threshold value for water, in the inner radius, was defined in relation  
222 to the pixel value with the maximum frequency in the slice according to the ratio of the  
223 lower threshold value of water and the pixel value with the maximum frequency in the  
224 central slice. The same procedure was applied for each material in each radius. The  
225 resultant segmented CBCT images using this procedure are referred to as  $sCBCT_{auto}$ .

226 The use of a radial shape was motivated by the fact that, in CBCT, the issue of the scatter



**Figure 1:** A slice of the pCT (a) and the original CBCT (b) and the resultant images after segmentation CBCT using the manual MLT ( $sCBCT_{man}$ ) and the automated MLT ( $sCBCT_{auto}$ ) (c and d respectively).

227 occurs spherically and ring artefacts that caused by miscalibrated detector pixel lines/rows,  
228 elements or manufacturing defects at a fixed location in the flat panel detector (FPD). In  
229 addition, due to the presence of the bilateral hip, the low energetic X-rays are absorbed,  
230 thus the polychromatic beam becomes gradually harder. Consequently, the FPD exhibits  
231 pixel-to-pixel sensitivity variations, that lead to ring artefacts (17). In a pelvic region with  
232 prostheses, there is a rapid change in the exposure to the FPD from frame to frame,  
233 receiving high exposure then followed by low exposure due the strong attenuation of the  
234 metal. This leads to so-called radar artefacts that appear as a circular radar bright-shaded  
235 region, owing to inconsistencies in detector signal and/or gain (18).

## 236 **2.4 Monte Carlo calculation**

237 The Elekta Synergy linear accelerator was modeled using Electron Gamma Shower  
238 (EGSnrc), which is one of the most popular MC codes for medical physics (19). BEAMnrc  
239 and DOSXYZnrc are two applications in EGSnrc code that are used to simulate the beam  
240 generated from the treatment head and to score dose deposition in voxel grids, respectively.  
241 In this study, 90 million particles were used for each beam to provide an accurate  
242 simulation with a low statistical uncertainty. High performance computing (HPC-Wales)  
243 was used to speed up MC calculations (20). The MC normalization was performed by  
244 calculating the dose in a water phantom under the standard reference conditions (10 ×10  
245 field size, 100 cm source-to-surface distance, 5 cm depth).

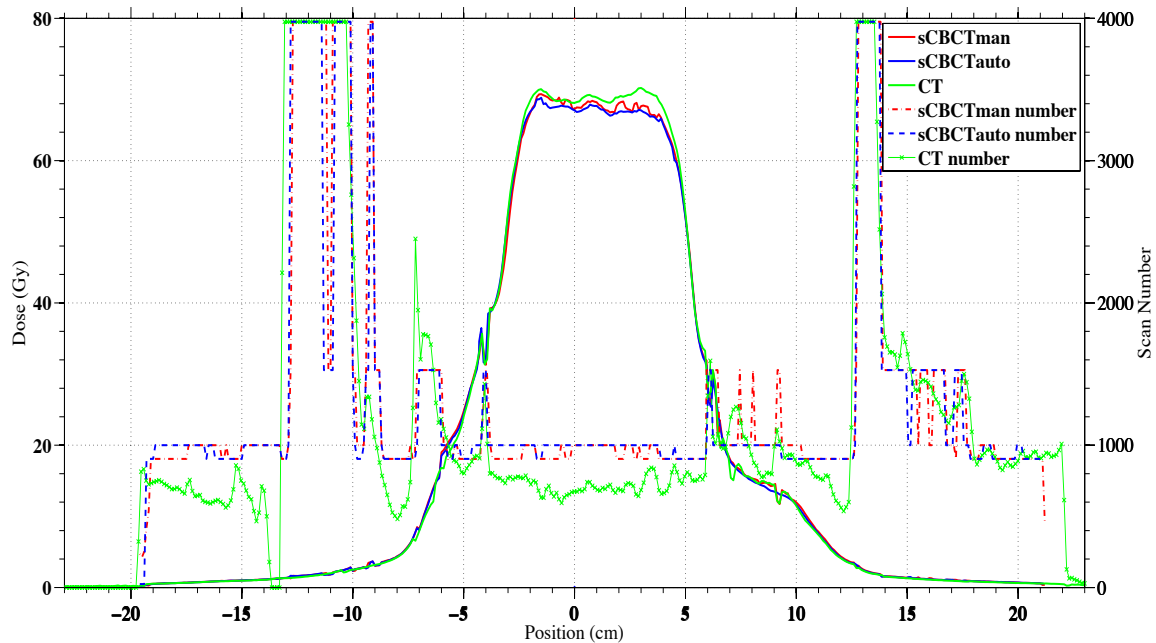
## 246 **2.5 Treatment planning evaluation and comparison**

247 The sCBCT (both sCBCT<sub>man</sub>, sCBCT<sub>auto</sub>) and pCT images fusion was accomplished with

248 manual rigid registration using ProSoma software (v3.3, MedCom, Germany) and the  
249 structure sets were then transferred to the sCBCT images without any modification except  
250 the external contour. The plans were then copied to sCBCT using the same geometry and  
251 MU values and doses were recalculated using PB and CC algorithms. For MC calculation,  
252 the pCT artefacts, caused by the presence of the hip prostheses, were changed to a water  
253 material of uniform density using a MATLAB script. The MC dose calculation was then  
254 performed on pCT and sCBCT images using the same HU-ED calibration as in OMP. The  
255 MC dose file (.3ddose) and the DICOM-RT file were then imported into the computational  
256 environment for radiotherapy research (CERR) software to compare the resultant dose  
257 distribution (21). Dose volume histograms (DVH) were compared between pCT and  
258 sCBCT plans. The maximum dose ( $D_{\max}$ ), mean dose ( $D_{\text{mean}}$ ) and minimum dose ( $D_{\min}$ )  
259 parameters for PTV (prostate and seminal vesicles), rectum and bladder were compared.  
260 The coverage of the PTV, the dose to 95% of the PTV ( $D_{95\%}$ ) and the relative volume  
261 doses delivered to the rectum and bladder ( $V_{65}$  and  $V_{70}$ ) were compared. In addition, the  
262 volume of right/left hip and bone were calculated in the pCT scan and compared with those  
263 in the sCBCT<sub>man</sub> and sCBCT<sub>auto</sub> scan to show how close the two scans were. To  
264 quantitatively appraise the differences between pCT and sCBCT plans, especially for the  
265 PTV, rectum and bladder, a gamma index analysis was performed using the pCT plan as a  
266 reference. The criteria were set as 3 mm distance to agreement (DTA) and 3% dose  
267 difference (DD) and 5% low dose threshold. The conformity index (CI) was calculated for  
268 all sCBCT plans and then compared with the pCT plans using PB, CC and MC algorithms  
269 (22). In addition, the dose at the isocentre (at the geometric centre of the prostate PTV  
270 (PTV<sub>p</sub>)) was compared between the pCT and sCBCT<sub>man</sub> and sCBCT<sub>auto</sub> plans.

271 **3 Results and discussion**

272 Figure 2 shows the cross-plane profile/x profile of pCT, sCBCT<sub>man</sub> and sCBCT<sub>auto</sub> at the  
 273 depth of the plan isocentre as well as the CT number of the pCT, sCBCT<sub>man</sub> and  
 274 sCBCT<sub>auto</sub> scans at that depth. In general, the sCBCT<sub>man</sub> and sCBCT<sub>auto</sub> profiles are in  
 275 good agreement with the pCT profile especially at the implant/tissue interface. For bone  
 276 regions, the sCBCT<sub>auto</sub> numbers showed less agreement with pCT numbers, compared with  
 277 sCBCT<sub>man</sub> numbers where some of these regions were considered as water. In addition, the  
 278 sCBCT<sub>auto</sub> overestimated some adipose tissue regions and considered it as water, especially  
 279 in the PTV region (high-dose region), leading to an underestimation of the dose in that  
 280 region by  $-4.4\%$ . On the other hand, sCBCT<sub>man</sub> numbers considered more adipose tissue

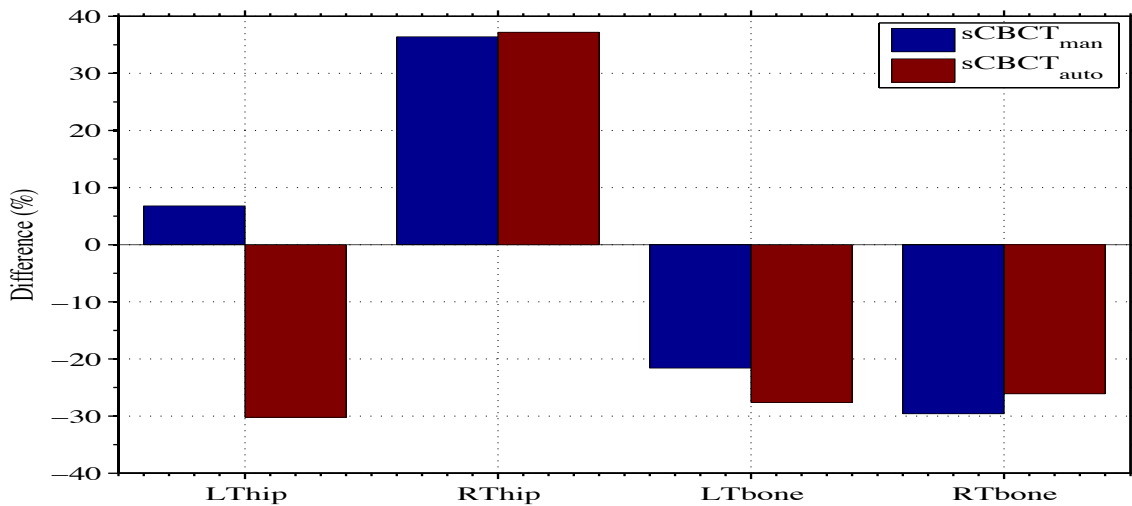


**Figure 2:** Comparison of the dose profile of pCT, sCBCT<sub>man</sub> and sCBCT<sub>auto</sub> plans at the isocentre depth using MC algorithm. The second y axis represents the sCBCT<sub>man</sub> number, sCBCT<sub>auto</sub> number and CT number.

281 than sCBCT<sub>auto</sub> numbers, thus the dose difference with the pCT dose profile was less when  
 282 compared with the sCBCT<sub>auto</sub> dose profile. The largest difference between the pCT and

283 sCBCT<sub>man</sub> and sCBCT<sub>auto</sub> plans was in the PTV region where pCT was 69.1 Gy,  
284 sCBCT<sub>man</sub> was 66.1 Gy and sCBCT<sub>auto</sub> was 65.8 Gy when using MC algorithm.

285 Figure 3 shows the differences in the right (RT)/left (LT) hip and bone volumes between  
286 the pCT scan, sCBCT<sub>man</sub> and sCBCT<sub>auto</sub> scans. Compared with the pCT scan, the largest  
287 difference between sCBCT<sub>man</sub> and sCBCT<sub>auto</sub> was found in the LT hip where in sCBCT<sub>man</sub>  
288 it was overestimated by 6.8% and underestimated by -30.2% in sCBCT<sub>auto</sub>. This  
289 underestimation was due to the fact that the automated MLT algorithm was unable to  
290 accurately correct cupping artefacts due to the increased amount of scatter and beam  
291 hardening inside the LT hip, resulting in dark streaks (17, 18). Thus, the automated MLT  
292 algorithm erroneously replaced the artefacts with bone HU values while the manual MLT  
293 correctly replaced the artefacts with metal HU values as shown in Figure (4). On the other  
294 hand, both MLT algorithms overestimated the RT hip where scatter and bright streak

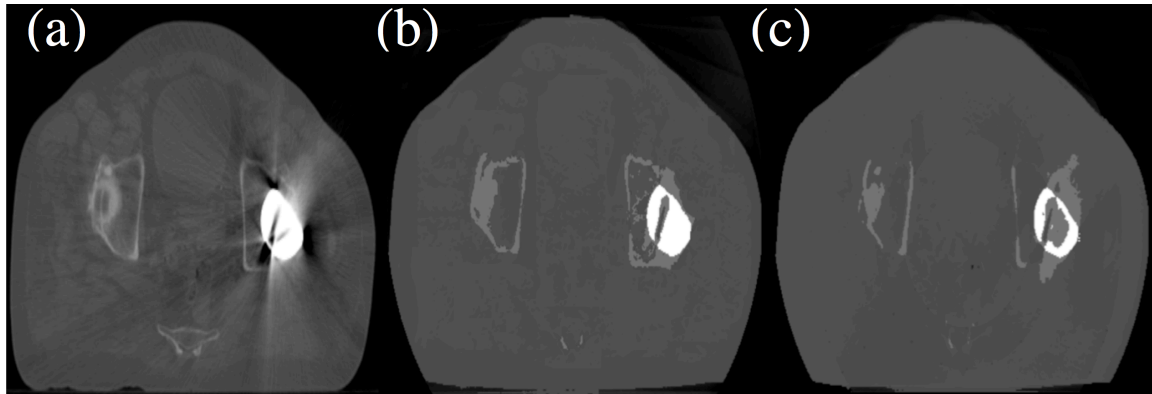


**Figure 3:** Right/Left hip and bone volume differences between pCT and sCBCT<sub>man</sub>/sCBCT<sub>auto</sub>.

295 artefacts were erroneously replaced with hip HU values, leading to a significant reduction  
296 in the RT bone volume around that region. Another reason for the underestimation of both

297 bone volumes in both MLT algorithms might be due to the fact that streak artefacts in pCT  
298 increased the number of high HU values and were not corrected (only for dose calculation),  
299 where in sCBCT, both MLT algorithms attempted to correct for this.

300



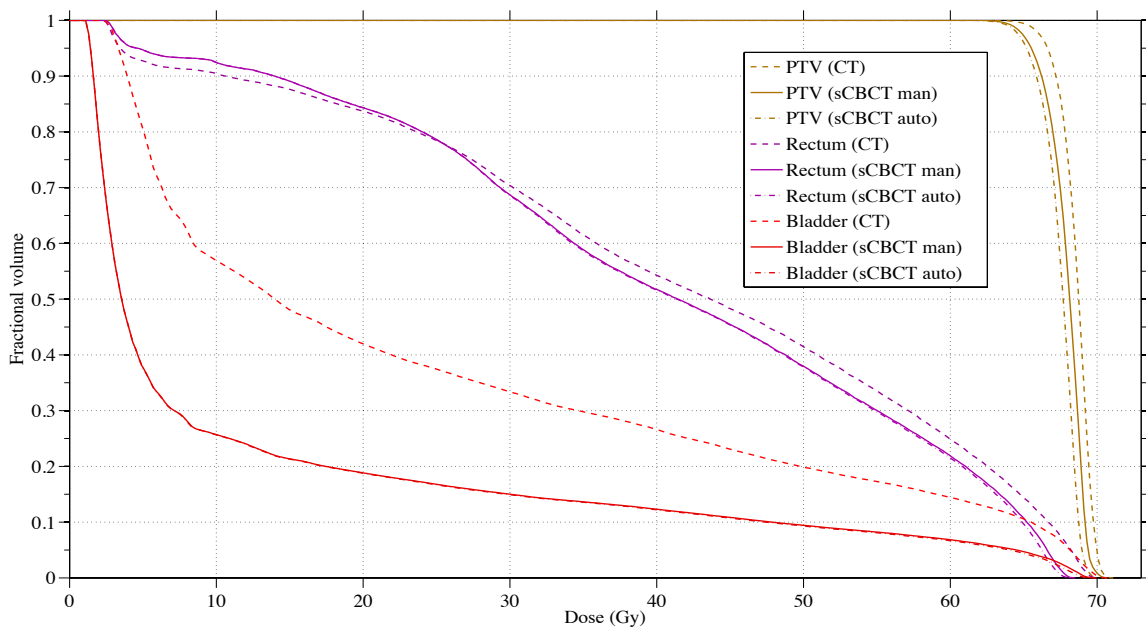
**Figure 4:** A slice of the pCT (a) and the resultant images after segmentation CBCT using the manual MLT ( $sCBCT_{man}$ ) and the automated MLT ( $sCBCT_{auto}$ ) (b and c respectively), showing the HU value difference in the left hip prosthesis.

301 Figure 5 shows the DVH of a prostate IMRT plan with a prescription dose of 70 Gy in  
302 35 fractions. It shows the dose of the pCT,  $sCBCT_{man}$  and  $sCBCT_{auto}$  plans to the PTV,  
303 rectum and bladder using the CC algorithm. Both  $sCBCT_{man}$  and  $sCBCT_{auto}$  plans showed  
304 almost the same difference from the pCT plan, except for the PTV where  $sCBCT_{man}$   
305 showed better agreement, the difference in  $D_{max}$  between the pCT and  $sCBCT_{man}$  plans  
306 was  $-0.56\%$ , and  $sCBCT_{auto}$  was  $-1.4\%$ . Compared with the pCT plan, the  $sCBCT_{man}$  plan  
307 underestimated  $D_{mean}$  and  $D_{min}$  by  $-1\%$  and  $-0.3\%$ , respectively, while the  $sCBCT_{auto}$  plan  
308 underestimated  $D_{mean}$  and  $D_{mean}$  by  $-1.6\%$  and  $-1\%$ , respectively. The MC and PB  
309 algorithm showed similar results to CC algorithm (see Table 1 in the Appendix 1).  
310 Compared with pCT plan, the bladder V65 was reduced by 56% and 58% in  $sCBCT_{man}$   
311 and  $sCBCT_{auto}$  plans, respectively, when using CC algorithm, showing better bladder  
312 sparing (Table 1). There was a tradeoff in the  $D_{95}$  of the PTV, which reduced by 9% and



313 14% in sCBCT<sub>man</sub> and sCBCT<sub>auto</sub> plans, respectively, when using the CC algorithm.  
 314 Significant organ deformation was observed between the pCT and CBCT scans, especially  
 315 in the bladder volume (>15% reduction). This deformation resulted in large differences in  
 316  $D_{\text{mean}}$  for the bladder in both sCBCT<sub>man</sub> (-48.8%) and sCBCT<sub>auto</sub> (-49.2%).

317 Previous studies used either deformable electron density or deformable image  
 318 registration (DIR) to improve the dose calculation accuracy and to correct the uncertainty  
 319 from organ deformation (11, 14). For a standard prostate patient, the accuracy of dose  
 320 calculation could be improved by 1-2% using these methods. Thor et al (2011) stated that  
 321 the accuracy of DIR can be affected by bowel gas and artefacts from gold fiducial markers



**Figure 5:** DVHs comparison pCT (-), sCBCT<sub>man</sub> (-) and sCBCT<sub>auto</sub> (-) IMRT plans for PTV, rectum and bladder using CC algorithm.

322 inside the prostate (23). Thus, in some cases, DIR would result in no improvement in the  
 323 accuracy of the dose calculation (14). In this study, the image quality of both pCT and  
 324 sCBCT images was affected by streak artefacts caused by the presence of the bilateral hip

325 prostheses, thus the uncertainty associated with using DIR would be increased.

326 Table 1: PTV coverage for the pCT, sCBCT<sub>man</sub> and sCBCT<sub>auto</sub>. The dose to 95% of PTV volume  
 327 and minimum dose and the percentage of rectal and bladder volumes receiving 65 Gy and 70 Gy.

| Scan                  |    | PTV  |      | Rectum |      | Bladder |      |
|-----------------------|----|------|------|--------|------|---------|------|
|                       |    | D95  | Dmin | V65    | V70  | V65     | V70  |
| CT                    | PB | 68.1 | 64.9 | 17.4   | 0.93 | 11.4    | 3.38 |
|                       | CC | 66.6 | 61.9 | 14.36  | 0    | 10.57   | 0.35 |
|                       | MC | 64.7 | 55.9 | 13.78  | 0    | 7       | 0    |
| sCBCT <sub>man</sub>  | PB | 66.4 | 62.5 | 12.83  | 0    | 5.13    | 0.52 |
|                       | CC | 65.5 | 61.7 | 10.74  | 0    | 4.6     | 0    |
|                       | MC | 64.7 | 55.9 | 10.36  | 0    | 4.2     | 0    |
| sCBCT <sub>auto</sub> | PB | 66.2 | 62.1 | 12.25  | 0    | 4.96    | 0.3  |
|                       | CC | 65.2 | 61.3 | 9.66   | 0    | 4.39    | 0    |
|                       | MC | 64.5 | 53.5 | 9.26   | 0    | 4.01    | 0    |

328

329 Dunlop et al (2015) eliminated the need for, and uncertainties associated with, DIR by  
 330 acquiring pCT on the same day as the CBCT, to be used as the ground truth for dose  
 331 calculation (9). Thus additional doses could be delivered to the patients.

332 Figure 6(a) shows the CI values of the pCT, sCBCT<sub>man</sub> and sCBCT<sub>auto</sub> plans using PB,  
 333 CC and MC algorithms. In general, the differences in the CI values between pCT and  
 334 sCBCT<sub>man</sub> were smaller than those between pCT and sCBCT<sub>auto</sub> using all algorithms. The  
 335 difference of the CI values between pCT and sCBCT<sub>man</sub> were  $-26.7\%$ ,  $-42.8\%$  and  $-$   
 336  $15.6\%$  when using PB, CC and MC algorithms, respectively. On the other hand, the  
 337 difference of the CI values between pCT and sCBCT<sub>auto</sub> were  $-38.9\%$ ,  $-74.1\%$  and  $-46.9\%$   
 338 when using PB, CC and MC algorithms, respectively. However, according to the RTOG  
 339 guidelines, the CI values between 0.9 and 1 indicate that the target volume is not adequately  
 340 covered by the prescribed isodose with a minor violation, whereas CI values of less than

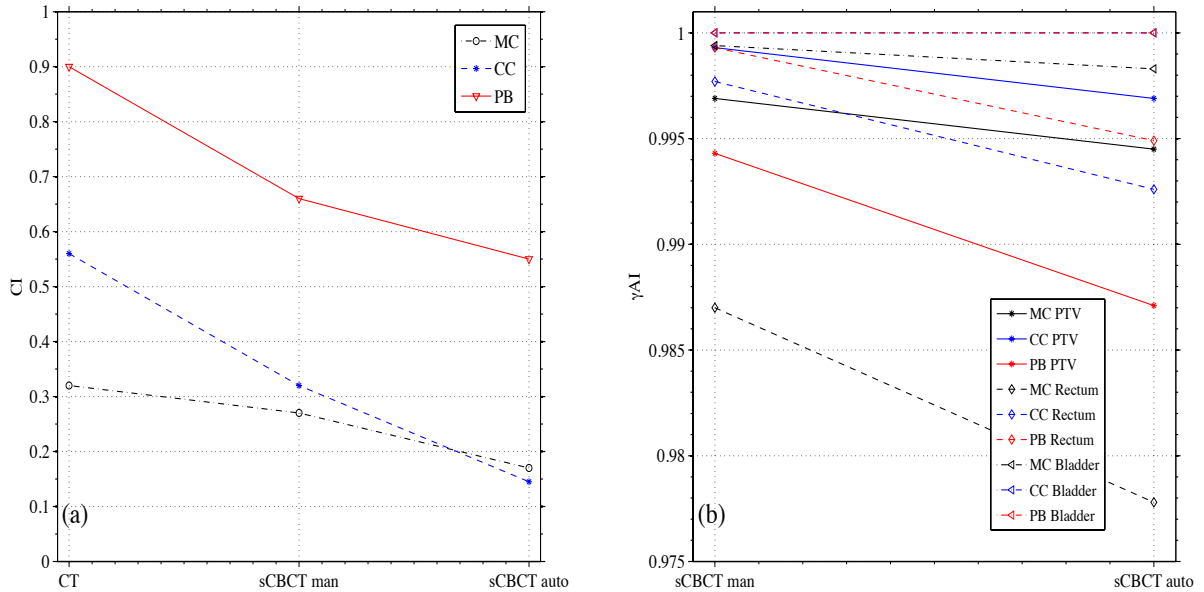


Figure 6: (a) Conformity index (CI) comparison between pCT, sCBCT<sub>man</sub> and sCBCT<sub>auto</sub> plans using PB, CC and MC algorithms. (b) Summary of the  $\gamma$  index with fixed DTA = 3 mm and DD = 3% for the calculation points falling inside the PTV, rectum and bladder, showing the fraction of points resulting with  $\gamma < 1$ .

341 0.9 the treatment plan are rated major violations but may nevertheless be considered to be  
 342 acceptable (24, 25).

343 Figure 6(b) shows the  $\gamma$  agreement index ( $\gamma$ AI) for the calculation points falling inside  
 344 the PTV, rectum and bladder for the pCT, sCBCT<sub>man</sub> and sCBCT<sub>auto</sub> plans, showing the  
 345 fraction of points resulting in  $\gamma < 1$ . For the bladder region, all the calculation points passed  
 346 the gamma test when using the PB and CC algorithm, while using the MC algorithm, 99.9%  
 347 and 99.8% showed  $\gamma < 1$  for sCBCT<sub>man</sub> and sCBCT<sub>auto</sub>, respectively. The lowest number  
 348 of points that passed was found in the rectum region when using MC algorithm, where  
 349 98.7% showed  $\gamma < 1$  in sCBCT<sub>man</sub> and 97.7% showed  $\gamma < 1$  in sCBCT<sub>auto</sub> plans, which is  
 350 clinically acceptable. Son et al stated that  $\gamma$  value is considered acceptable when the passing  
 351 rate is greater than 95% with 3 mm DTA and 3% DD criteria (26).

352 Table 2: Dose comparison between pCT, sCBCT<sub>man</sub> and sCBCT<sub>auto</sub> plans at the isocentre using  
 353 PB, CC and MC algorithms.

| Scan                | sCBCT <sub>man</sub> |       |       | sCBCT <sub>auto</sub> |       |       |
|---------------------|----------------------|-------|-------|-----------------------|-------|-------|
|                     | PB                   | CC    | MC    | PB                    | CC    | MC    |
| Dose difference (%) | -0.81                | -0.46 | -0.39 | -1.44                 | -1.36 | -1.39 |

354

355 Table 2 shows the dose difference between pCT and sCBCT plans at the isocentre using  
 356 all algorithms. In general, both sCBCT<sub>man</sub> and sCBCT<sub>auto</sub> plans showed differences of less  
 357 than  $-2\%$  compared with the pCT plan using all algorithms, which are both considered to  
 358 be clinically acceptable. It can be seen that the difference between the sCBCT<sub>man</sub> and  
 359 sCBCT<sub>auto</sub> is larger when using CC and MC algorithms than that when using the PB  
 360 algorithm. This is due to the fact that the PB algorithm in OMP calculates dose to water  
 361 while, the CC algorithm calculates dose to medium, as does the MC algorithm (27).  
 362 Therefore, the PB algorithm would be less sensitive than CC and MC for calculating the  
 363 dose using different scans. Thus MC and CC algorithms minimised uncertainty related to  
 364 the dose calculation as well as identifying those introduced by different scans. However,  
 365 for the MC calculation, the difference increased from  $-0.4\%$  in the sCBCT<sub>man</sub> plan to  $-$   
 366  $1.4\%$  in sCBCT<sub>auto</sub> plan when compared with the pCT plan. On the other hand, the operator  
 367 time required for defining the threshold values for different regions in sCBCT<sub>man</sub> was 8  
 368 hours while in sCBCT<sub>auto</sub>, the threshold values were defined automatically and takes 20  
 369 min operator time. Some manual modification to ensure an appropriate assignment of each  
 370 material in sCBCT<sub>auto</sub> scan was still needed to improve the accuracy but it requires much  
 371 less (approximately 95%) operator time compared with sCBCT<sub>man</sub> scan. Dividing CBCT  
 372 images into five concentric rings was accurate enough to correct the variation in the pixel

373 value with position in the CBCT images. As a result, the automated MLT algorithm  
374 reduced the operator time with an acceptable accuracy. This time saved could turn this  
375 technique from a research-based to a clinical implementation and makes it superior  
376 compared with the manual approach. Compared with the proposed technique in this paper,  
377 acquiring a new pCT is more time consuming, increase work load on physicists, physicians,  
378 and radiographers, which can take up to a day in a busy radiotherapy department, and more  
379 importantly additional dose is delivered to the patient.

#### 380 **4 Conclusion**

381 The segmentation of CBCT images using methods in this study can be used for dose  
382 calculation. For a prostate patient with bilateral hip prostheses, the MLT algorithms  
383 achieved a sufficient dose calculation accuracy that is clinically acceptable. The automated  
384 MLT algorithm reduced the operator time associated with the MLT algorithm, making it  
385 possible to implement the technique into clinic. Thus this method would be feasible for  
386 ART, as an alternative to obtaining a new planning CT and re-outlining the structures. This  
387 method can be applicable for dose calculation on MR images and could be of interest to  
388 MR-based ART.

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