Estimation of Hounsfield Unit conversion parameters for pelvic CT images

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25 **Acknowledgements**

26 This work was supported by the National Health and Medical Research Council of Australia
27 (NHMRC Project Grant 1077788). We are grateful to Prof James Denham and other
28 investigators of the TROG 03.04 RADAR trial.

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30

31 **Abstract**

32 Linear scaling is used to convert raw computed tomography (CT) pixel values into
33 Hounsfield units corresponding to different tissue values. Analysis of a benchmarking study,
34 presented here, where the same CT scan was imported into and then exported from multiple
35 radiotherapy treatment planning systems, found inconsistencies in HU scaling parameter
36 values exported along with the images, particularly when images were exported using the
37 Radiation Therapy Oncology Group (RTOG) format. Several methods of estimating
38 conversion parameters, based on estimating pixel values corresponding to air and water
39 within the image, for pelvic CT images from a large multi-centre trial were compared against
40 original Digital Imaging and Communications in Medicine (DICOM) export parameters. In
41 general using the mean of a sample region at the centroid of the bladder to estimate the value
42 of water was more accurate than using the minimum or maximum or a single value at the
43 centroid. Accuracy of methods of air estimation tested were dependent in part on features of
44 the CT scanners and treatment planning systems, making it difficult to pick one method as
45 superior that was independent of scanner and treatment planning system type. Based on the
46 above analysis, methods for estimating air and water were selected for use in performing
47 linear scaling of a set of pelvic CT images prior to their use in an interpatient image
48 registration application. The selected methods were validated against a more recent and
49 homogeneous dataset. Estimation error was found to be much lower within the validation set.

50 **Keywords:** Hounsfield units, linear scaling estimation, RTOG, DICOM, interpatient
51 registration

52

53 I. Introduction

54 The Radiation Therapy Oncology Group (RTOG; [1]) and Digital Imaging and
 55 Communications in Medicine (DICOM; [2]) data storage formats represent computed
 56 tomography (CT) image pixels as a list of integer (always unsigned for RT0G[3] and
 57 sometimes unsigned for DICOM[2]) values (referred to as raw pixel values throughout this
 58 report). Conversion from HU can be required to ensure that the range of pixel values will fit
 59 within the range of the datatype used during export. For example, when an unsigned integer
 60 is used shifting is often needed to ensure all values are positive. Scaling allows for
 61 adjustments to precision so can, for example, allow the preservation of floating point
 62 precision or reduce the number of bits required to store a particular range of values but with
 63 lower than unit precision. Linear parameters, provided in the image headers, are available for
 64 scaling the raw pixel values to Hounsfield Units (HU), with values of -1000 for air and 0 for
 65 water, enabling inter-patient identification of different tissue types. Having intensities for
 66 corresponding tissues match between image sets can also have an impact on applications
 67 requiring image registration when methods of image similarity calculation, such as the sum-
 68 of-squared differences (SSD) of pixel values, used during image registration rely directly on
 69 pixel intensity values. For the RTOG format [1,3] the conversion parameters provided are the
 70 raw pixel values corresponding to air, a , and water, w . A linear conversion is then applied to
 71 transform raw pixel value, x , to its HU value, $H(x)$:

$$72 \quad H(x) = -1000 + (x - a) * \frac{1000}{w-a} \quad (1)$$

73 In the case of the DICOM format the parameters [2] are the slope, s , and intercept, i , of a
 74 linear function:

$$75 \quad H(x) = s \cdot x + i \quad (2)$$

76 As part of an ongoing outcomes investigation, inter-patient registration of pelvic CT images
77 from the Trans-Tasman Radiation Oncology Group (TROG) 03.04 RADAR (Randomised
78 Androgen Deprivation And Radiotherapy) trial [4] is being performed. In many cases raw
79 pixel values to HU conversion parameters have been lost as part of the database upload
80 process or are inconsistent [5] and so must be estimated from features within the images. The
81 aim of this study is to present and compare several automated methods of performing
82 parameter estimation in the context of subsequent image registration based dose-outcomes
83 analyses. To our knowledge this issue has not been previously addressed. Although CT
84 conversion parameters were estimated by Chang et al [5] the estimation methods were not
85 automated and no evaluation of estimation accuracy was reported.

86 II. Methods and Materials

87 *Evaluation of errors in original RADAR parameters*

88 A previous investigation relating CT HU of patients to muscle attenuation found that raw
89 pixel to HU conversion parameters were sometimes inconsistent for a subset of patients in the
90 RADAR dataset [5]. A benchmarking study [4], performed as part of the quality assurance
91 process for the RADAR trial, compared the results of contours delineated on the same
92 DICOM CT set for participating trial centres using their own treatment planning system. As a
93 result, the same CT set was available after export from the scanner that was used to create the
94 images plus 13 different trial centres in either RTOG or DICOM format (depending on the
95 trial centre and planning system). All DICOM exports apart from the original CT export,
96 which came directly from a Light Speed Plus CT scanner, were exported using Eclipse
97 (version 7.2.24 or 7.3). Information about the treatment planning system was not recorded in
98 the RTOG exports so it is not known which TPS or TPS version was used for each export,

however the participating centres were known to have used XIO (versions 4.1.1, 4.2.2, 4.3.1 or 4.3.3), Pinnacle (versions 6.06, 6.2b, 7.6c or 8.0d) or Eclipse (versions 6.5, 7.1.67, 7.2.24, 7.3, 7.3.1 or 8) over the time that they participated in the trial. The consistency of resulting exported raw pixel values and linear parameters provided some indication of the reliability of the original parameters, which is important for the interpretation of comparisons with estimated parameters described below.

Comparison with original RADAR parameters

Parameter estimation was performed for CT for 711 prostate cancer patients treated across 23 centres during 2003-2008 during the RADAR trial [4] and archived to the SWAN software system [6]. As part of the treatment planning process these images had been imported into commercial treatment planning systems before being re-exported in RTOG or DICOM format. Bladder structures, outlined as part of the treatment planning process and reviewed by three experts, were available for all datasets. As a result of the upload process used by SWAN at the time CT-HU conversion information was lost for most image sets. Original RTOG exports for 101 of the RADAR treatment plans and original DICOM RT exports for 45 of the RADAR treatment plans were available for comparison with estimated parameters. In the case of the DICOM exports the slope and intercept parameters were used to find the raw image intensity values corresponding to air and water, which were then compared to the estimated values of air and water.

Comparison with original parameters from an external dataset

The inconsistency in parameter interpretation for the RADAR dataset (as established by the analysis of benchmarking data) makes it desirable to evaluate parameter estimation accuracy on a more consistent dataset. A comparison for the methods of air and water estimation we

ultimately selected for use in our interpatient registration application (methods a1 and w2) was performed against a more recent dataset. Pelvic CT scans for 42 prostate cancer patients[7] attending the Calvary Mater Newcastle Hospital, New South Wales, Australia, were available for this purpose (referred to as the NC set). These images were generated on two CT scanners and exported from the same treatment planning systems into DICOM RT. Parameters were estimated for 42 CT images from the NC dataset that had already been converted to HU after export from the treatment planning system. Estimated values for air and water were compared to the standard HU values of -1000 for air and 0 for water.

Parameter Estimation

Conversion from raw pixel values to HU in RTOG is via a linear transformation based on knowing the raw pixel values corresponding to air and water. The approach to parameter estimation evaluated here was to find a way of locating and sampling air and water in the images.

It was assumed that the lowest attenuation within the field of view (FOV) was that of air outside the body. The raw pixel value of air could correspond to the minimum raw value in the CT image with a frequency greater than 100 or to the value of a point on the image, identified as being reliably outside the body and avoiding padding, table and scanner pixels.

It may also be desirable to take a sample over a region rather than sampling an individual pixel to account for noise and possible artefacts in the image that could create a small number of extreme values. Estimation of water, in a patient imaged without contrast, is based on the assumption that the pixels in and around the geometric bladder centroid correspond to water. Urine has been found to have a specific gravity relative to water ranging from 1.002 to 1.037[8] so has a density very close to that of water. The HU of urine was reported to range from 5 to 15 [9] and Mizumura et al[10] found that ascites of patients with bladder ruptures

have a median HU of 5.7 (range of 3.1 to 6.1) so it is expected to provide a reasonable approximation of water. Table 1 outlines 3 methods tested for air estimation and 4 methods tested for water estimation based on the above assumptions. The choice of air sampling location used for methods a2 and a3 (see table 1) was based initially on examination of the common locations for air in a subset of the images. When running comparisons to original parameters, any cases where a2 and a3 results were a lot worse than a1 were manually checked and, where sampling location was an issue, used to adjust how the location was selected before comparisons were re-run. Similarly initial tests of using a1 without the frequency-greater-than-100 condition showed occasional extreme errors due to very low frequency noise, which led us to introduce the condition. For methods sampling pixels from a region centred on a sampling location we chose a small sample size of 3 pixels in each dimension (27 in total). The risk of using a large sample size is that if, for example, the bladder is an unusual shape pixels may be included in the sample that are near the edge or outside of the bladder.

Table 1 Methods for performing air and water estimation. Method a1 is based on finding minimum pixel values. Methods a2 and a3 and w1-w4 are based on sampling a pixel or a sample of pixels from a particular region

Estimate		Sampled Pixels	Estimate Calculation
Method			
air	a1	All pixels considered	minimum pixel value with frequency > 100*
	a2	3x3 region centred on the middle column and 3rd	mean pixel value

	a3	row of the 2nd CT slice	minimum pixel value
water	w1	The single pixel closest to the centroid** of the outlined bladder structure	value of the centroid pixel
	w2	3x3 pixel region centered on the centroid of the outlined bladder structure	mean of the sampling region
	w3		minimum of the sampling region
	w4		maximum of the sampling region

164 * the “frequency > 100” condition is intended to avoid small amounts of noise from being used to estimate air

165 ** calculated as the average location of all the pixels that were inside the delineated bladder structure

166 II. Results

167 *Evaluation of errors in original RADAR parameters*

168 Tables 2 and 3 provide a comparison of exported raw pixel values and linear parameters
169 provided by each system upon exporting the benchmarking CT scan using RTOG (11
170 centres) and DICOM (3 centres + the original DICOM benchmark CT set) format
171 respectively. Columns 2 and 3 provide parameters retrieved from the image file headers. The
172 remaining columns provide statistics for values sampled from the raw pixel images. In Table
173 2 scaling values provided for air and water sometimes differ despite raw pixel values being
174 unchanged (rows 2-6). For example the values of -976 for air and 1029 for water in row 3 are
175 clearly incorrect as they would mean there was no air in the image. For 2 centres (row 1)
176 parameters were the same as for 5 other centres (row 2) but raw values in the centre of the
177 body region and bladder had been shifted in comparison to the images exported from all other
178 centres whilst the minimum raw value outside the body as measured by a1 and a3 remained
179 the same.

The interpretation of the DICOM conversion parameters as summarised in Table 3 is more consistent. Only the original CT image export (row 2) is inconsistent with the exports for the trial centres. The samples taken from the body region match but the minimum pixel value with frequency greater than 100 as well as the sample taken from outside the body (a2 & a3) region, presumably corresponding to air do not. A difference image comparing intensity values in the original CT image (row 2) vs one of the DICOM exports created by a TPS (row 1) showed that noise like differences were present anywhere that corresponded to air including air pockets within the body region. This could potentially lead to error in air value estimation. If original parameters are available then values within the body will at least remain consistent between datasets since the slopes and intercepts provided are consistent between DICOM exports and pixels sampled from within the patient body match exactly. The parameters provided with the DICOM exports are always at least slightly inconsistent with all of the RTOG exports since none of the RTOG air and water parameter pairs provided would equate to a slope of 1.0 if converted to DICOM parameters.

Table 2 Features of the benchmark CT scan after import and export by different trial centres into RTOG format.

	RTOG export		Raw pixel value samples							Perfect match between centre pixels*?
	parameters		a1	a2	a3	w1	w2	w3	w4	
Centres producing these values										
2	0	1024	0	10	0	1052	1005	952	1065	No
5	0	1024	0	23	0	1076	1029	976	1089	Yes

1	-976	1029	0	23	0	1076	1029	976	1089	Yes
1	17	998	0	23	0	1076	1029	976	1089	Yes
1	17	999	0	23	0	1076	1029	976	1089	Yes
1	24	1028	0	23	0	1076	1029	976	1089	Yes

* raw pixel values in a 100 pixel cubed region at the centre of the image are compared to corresponding pixels in the original CT scan

Table 3 Features of the benchmark CT scan after import and export by different trial centres into DICOM format. The original CT set (corresponding to the second data row) provided to trial centres was in DICOM format and is included the comparison.

	DICOM export parameters		Raw pixel value samples							
	Slope	Intercept	a1	a2	a3	w1	w2	w3	w4	Perfect match between centre pixels?
Centres producing these values										
3	1	-1024	24	34	24	1076	1029	976	1089	Yes
1*	1	-1024	0	23	0	1076	1029	976	1089	Yes

* This row corresponds to the original CT set that was imported and then exported by each of the participating centres.

Comparison with original RADAR parameters

Figures 1 and 2 present box and whiskers plots summarising differences between estimated and original values for air and water for images exported to DICOM only. A positive value along the vertical axis corresponds to the case where the estimated value of air or water is

higher than the original value calculated based on the slope and intercepts present in the original DICOM header. The comparisons are restricted to DICOM image sets due to the inconsistencies found for RTOG in the benchmarking data and improbably extreme errors found in initial RTOG comparisons for air. Air estimation method a2 has the lowest average absolute error of 4.49 (sd=7.5). However the presence of noise or artefacts in the sampling region for some images means that at times the method fails by up to 49 units. Method a3 has a slightly higher average absolute error of 5.27 (sd=8.0) but lower maximum error of 40 raw pixel values. Method a1 (mean=12.8, sd=12.11) is very consistent, either being accurate with zero error or being exactly +-24 units out and avoids the need for selecting a sampling region.

Fig. 1 Box and whiskers plots showing the distribution of air estimation errors for different estimation methods. The mean values correspond to the diamonds linked by the dotted line. Only images exported to DICOM (n=45) are included. For a1_RADAR the minimum, 1st quartile and median are all -24. For a3_RADAR the mean and the 3rd quartile are both zero.

Fig. 2 Box and whiskers plots showing the distribution of water estimation errors for different estimation methods. The mean values correspond to the diamonds linked by the dotted line. Only images exported to DICOM are included. The first 4 series show error estimation values for the RADAR subset (n=45) where original values were available the last corresponds to error estimation for the Newcastle dataset (n=42)

The results for the water comparison (Fig. 2) have a noticeably higher error range than for air. The average of the centroid region, estimation method w2 (absolute error mean=15.22, sd=15.96), is consistently closer to the original value for water than other methods (absolute error means ranging from 18.49 to 42). There is a positive bias in estimation error for all methods except w3 (error means: w1=15.47, w2=13.62, w3=-16.07, w4=42), which takes the minimum of the sample region and a moderate negative

correlation between bladder volume and estimation error for most methods of estimation (correlation coefficients $r_{w1}=-0.23$, $r_{w2}=-0.44$, $r_{w3}=-0.33$, $r_{w4}=-0.48$, $r_{w2_NC}=-0.29$).

Comparison with original parameters from an external dataset

Estimation error was generally much lower for the NC set than the RADAR set. The estimation error for air using method a1 was 0 for all images. Mean error in estimation of water using method w2 was 3.74 (sd=10.66) and the mean of the absolute error was 8.74 (sd=7.05). The range of estimation error was -23 to 25. Fig. 2 displays a summary of the distribution of error in w2 estimation for NC (w2_NC) compared to water estimation errors using methods w1-w4 for RADAR. If the assumption that conversion into HU for this dataset was correct holds then this distribution provides an estimate of the expected HU distribution of urine.

IV. Discussion

Analysis of the benchmarking CT set suggests that scaling parameters to convert CT images from raw image intensity values to Hounsfield Units recorded in radiotherapy plan exports have not always been consistently interpreted, especially for the RTOG format. The order of magnitude of errors found in parameter interpretation for RTOG exports and in parameter estimation for the RADAR dataset was high enough to potentially interfere with identification of different types of soft tissue. For example an HU value of 50 as calculated using the slope and intercept provided with the original benchmarking CT set would, when converted using parameters exported to RTOG by other trial centres, be assigned CT numbers ranging from 22 to 77. A value of -100 would be assigned an HU number ranging from -103 to 61. This magnitude of error could have implications for applications involving data-mining

of older radiation oncology clinical imaging information (e.g. data-linkage for decision support systems [11] or radiomics [12]).

Several methods were compared for the estimation of raw pixel values of air and water for a heterogeneous multi-centre pelvic CT dataset. Using the mean of a sample of pixels at the centre of the bladder worked better for water estimation than use of a single value at the centroid or the maximum or minimum values of the sample region. On average the best water estimation method was 13.62 raw units too high. Given that the range of HU found to correspond to urine (without contrast) ranges from -5 to 15 [9] it may be appropriate to use bladder estimates to directly estimate a urine HU of 5. The moderate negative relationship of water estimation error with bladder volume is consistent with the positive relationship previously found between urine concentration and HU [13,14]. Estimation accuracy could potentially be further improved by adjusting the expected HU of urine based on bladder volume.

The mean error for estimation of air was generally lower than for estimation of water. The best choice of estimation method when compared against original DICOM parameters appears to depend on the particular dataset estimation is being applied to. The suitability of the different methods for air estimation within a particular dataset depended on noise in the image and artefacts surrounding the image. The estimates based on a mean of the selected sampling location (a2) resulted in the lowest average error. However the error range was higher than for method a1, where the need to select a sampling location could be avoided. The fact that the estimated value is so often out by exactly 24 when method a1 is used is odd but may be related to the differences in export parameter interpretation. When comparing the same image exported to DICOM by Eclipse versions 7.2.24 and 7.3 vs the original export from the Light Speed Plus CT scanner we found that despite identical slope, intercept, and

pixel values sampled from within the body there were differences in pixels outside the body and minimum pixel value difference of exactly 24.

Validation of the chosen methods a1 and w2 was performed for the more homogenous NC dataset, where we had higher confidence that the original conversion into HU was consistent and correct. In this case average estimation errors were much lower at 0 raw units for air and 3.73 raw units for water, providing more confidence that methods a1 and w2 are suitable for application to the RADAR image set. Given that the NC dataset was already converted into HU before these estimates were made the values sampled, which also correspond to the error, could be assumed to provide an estimate of urine HU. Whilst the mean at 3.74 is consistent with the mean HU of ascites created by bladder ruptures[10] the range of -23 to 25 was somewhat higher adding to the uncertainty of parameter estimates for any individual dataset.

Chang et al[5] commented that their methods of using estimated air and water attenuation values in normalisation of the images should be tested on images exported to DICOM RT format presumably with the intention of evaluating the accuracy of their methods. Given that the underlying assumptions made in this study, that pixels outside the body correspond to air and pixels near the centroid of the bladder correspond to water, match those made by Chang et al these results may be useful in indicating the expected uncertainty in their parameter estimates. One caveat is that in their case sampling locations were selected manually so were less vulnerable to potential problems with choice of sampling location.

Overall the impact of estimation errors on retrospective dose-outcomes analysis depends on the image processing methods performed. For the application of inter-patient registration between RADAR images (useful in facilitating automatic segmentation of structures[15] or voxel based comparisons of planned dose between patients for subsequent dose outcomes analysis) the impact of linear scaling error is likely to be dependent on the image similarity

metrics used. Some metrics such as the sum-of-squared differences are highly dependent on absolute pixel values whereas others such as normalised cross-correlation or normalised mutual-information are insensitive to or independent of linear scaling[16]. For image sets where linear scaling parameters are not available or may not be reliable, as was the case for the RTOG exports in the RADAR trial, parameter estimation can be used. Where possible, care should also be taken in selection of image processing methods that reduce linear dependence on pixel intensities.

V. Conclusions

Analysis of benchmarking data established that exported linear parameters for converting raw CT values to Hounsfield Units are not always consistently used. In situations where legacy data is being used in image intensity sensitive analyses we recommend that a check is made to confirm that converted intensity values are within an expected range for identified tissue types.

In lieu of exported RTOG or DICOM HU conversion parameters or in the case where parameters are shown to be inaccurate using either methods a1, based on minimum pixel values and showing zero error in the validation dataset, or a2, based on the mean of an area sampled outside the body and showing the lowest mean error when compared to original values of the RADAR dataset, to estimate the raw CT value of air and method w2 based on the mean of sampled bladder pixels for estimating the raw CT value of water will provide a close approximation of appropriate conversion parameters. If high levels of accuracy are required then modifying the linear conversion equation to use estimated urine HU values instead of water and adding an adjustment based on bladder volume may be preferable.

Compliance with Ethical Standards

325 Funding: This work was supported by the National Health and Medical Research Council of
326 Australia (NHMRC Project Grant 1077788)

327 Conflict of Interest: We are aware of no conflicts of interest by any of the authors.

328 Ethical approval: This article does not contain any studies with animals performed by any of
329 the authors. All procedures performed in studies involving human participants were in
330 accordance with the ethical standards of the institutional and/or national research committee
331 and with the 1964 Helsinki declaration and its later amendments or comparable ethical
332 standards.

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References

1. Baxter BS, Hitchner LE, Maguire Jr GQ (1982) A standard format for digital image exchange. American Institute of Physics, New York N.Y.
2. NEMA (2001) Digital Imaging and Communications in Medicine (DICOM). Part 3: Information Object Definitions. Standard Office of Publications, Washington DC
3. Harms W (1999) Specifications for Tape/Network Format for Exchange of Treatment Planning Information. RTOG 3D Quality Assurance Center, Washington University. http://itc.wustl.edu/exchange_files/tapeexch400.htm#ch6. Accessed 02 April 2018
4. Kearvell R, Haworth, A., Ebert, M. A., Murray, J., Hooton, B., Richardson, S., Joseph, D. J., Lamb, D., Spry, N. A., Duchesne, G. and Denham, J. W. (2013) Quality improvements in prostate radiotherapy: Outcomes and impact of comprehensive quality assurance during the TROG 03.04 'RADAR' trial. J Med Imag Radiat Oncol 57:247-257. doi:10.1111/1754-9485.12025
5. Chang D, Joseph DJ, Ebert MA, Galvão DA, Taaffe DR, Denham JW, Newton RU, Spry NA (2014) Effect of androgen deprivation therapy on muscle attenuation in men with prostate cancer. J Med Imag Radiat Oncol 58 (2):223-228. doi:10.1111/1754-9485.12124
6. Ebert MA, Haworth A, Kearvell R, Hooton B, Coleman R, Spry N, Bydder S, Joseph D (2008) Detailed review and analysis of complex radiotherapy clinical trial planning data: Evaluation and initial experience with the SWAN software system. Radiother Oncol 86 (2):200-210. doi:<http://dx.doi.org/10.1016/j.radonc.2007.11.013>
7. Dowling JA, Sun J, Pichler P, Rivest-Hénault D, Ghose S, Richardson H, Wratten C, Martin J, Arm J, Best L, Chandra SS, Fripp J, Menk FW, Greer PB (2015) Automatic Substitute Computed Tomography Generation and Contouring for

- 360 Magnetic Resonance Imaging (MRI)-Alone External Beam Radiation Therapy From
 361 Standard MRI Sequences. *Int J Radiat Oncol Biol Phys* 93 (5):1144-1153.
 362 doi:10.1016/j.ijrobp.2015.08.045
- 363 8. Rose C, Parker A, Jefferson B, Cartmell E (2015) The Characterization of Feces
 364 and Urine: A Review of the Literature to Inform Advanced Treatment Technology.
 365 *Critical Reviews in Environmental Science and Technology* 45 (17):1827-1879.
 366 doi:10.1080/10643389.2014.1000761
- 367 9. Lepor H (1999) Prostatic Diseases. W.B. Saunders Company, St. Louis
- 368 10. Mizumura N, Okumura S, Toyoda S, Imagawa A, Ogawa M, Kawasaki M (2017)
 369 Non-traumatic bladder rupture showing less than 10 Hounsfield units of ascites.
 370 *Acute Medicine & Surgery* 4 (2):184-189. doi:doi:10.1002/ams2.248
- 371 11. Lambin P, Roelofs E, Reymen B, Velazquez ER, Buijsen J, Zegers CML,
 372 Carvalho S, Leijenaar RTH, Nalbantov G, Oberije C, Scott Marshall M, Hoebbers F,
 373 Troost EGC, van Stiphout RGPM, van Elmpt W, van der Weijden T, Boersma L,
 374 Valentini V, Dekker A (2013) 'Rapid Learning health care in oncology' – An approach
 375 towards decision support systems enabling customised radiotherapy'. *Radiother*
 376 *Oncol* 109 (1):159-164. doi:<https://doi.org/10.1016/j.radonc.2013.07.007>
- 377 12. Lambin P, Rios-Velazquez E, Leijenaar R, Carvalho S, van Stiphout RGPM,
 378 Granton P, Zegers CML, Gillies R, Boellard R, Dekker A, Aerts HJWL (2012)
 379 Radiomics: Extracting more information from medical images using advanced
 380 feature analysis. *Eur J Cancer* 48 (4):441-446.
 381 doi:<https://doi.org/10.1016/j.ejca.2011.11.036>
- 382 13. Zwingenberger AL, Carrade Holt, Danielle D. (2017) Computed tomographic
 383 measurement of canine urine concentration. *CANADIAN VET J* 58 (2):180-182

- 384 14. Hsu CT, Wang ZJ, Yu ASL, Gould RG, Fu Y, Joe BN, Qayyum A, Breiman RS,
385 Coakley FV, Yeh BM (2008) Physiology of Renal Medullary Tip Hyperattenuation at
386 Unenhanced CT: Urinary Specific Gravity and the NaCl Concentration Gradient.
387 Radiology 247 (1):147-153. doi:10.1148/radiol.2471070585
- 388 15. Acosta O, Dowling J, Drean G, Simon A, de Crevoisier R, Haignon P (2014)
389 Multi-Atlas-Based Segmentation of Pelvic Structures from CT Scans for Planning in
390 Prostate Cancer Radiotherapy. In: El-Baz AS, Saba L, Suri J (eds) Abdomen and
391 Thoracic Imaging: An Engineering & Clinical Perspective. Springer US, Boston, MA,
392 pp 623-656. doi:10.1007/978-1-4614-8498-1_24
- 393 16. Derek L.G. Hill PB (2001) Registration Methodology: Concepts and Algorithms. In:
394 Joseph V. Hajnal DLGH, David J. Hawkes (ed) Medical Image Registration. The
395 Biomedical Engineering Series. CRC Press, Boca Raton London New York
396 Washington, D.C.,
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Figure_1

Figure_2