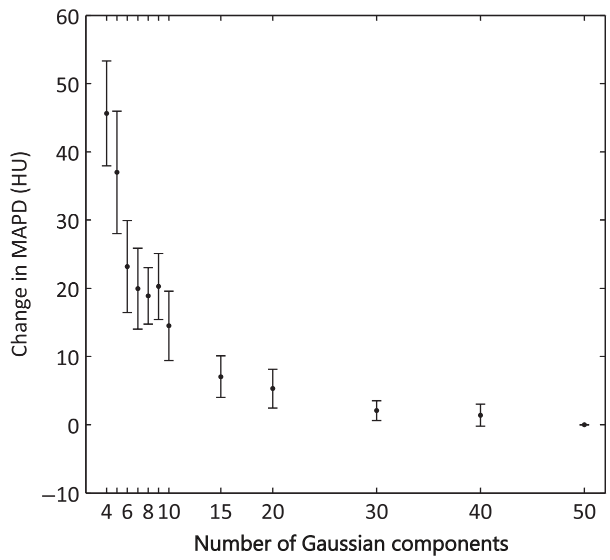
Supplementary material for Johansson A. et al. Improved quality of computed tomography substitute derived from magnetic resonance (MR) data by incorporation of spatial information – potential application for MR-only radiotherapy and attenuation correction in positron emission tomography, Acta Oncol 2013; 52:1369–1373.



Supplementary Figure 1. Change in MAPD with respect to the number of components. N = 50 is used as reference. The bars show 95% confidence intervals with respect to the reference.

Supplementary Table I. Effect of spatial standard deviation on MAPD.

λ_i (mm)	95% confidence interval for change in MAPD (HU)
1	[−1.6, 1.9]
2	[−0.6, 1.7]
5	[−0.8, 1.5]
10	–
20	[−0.1, 2.9]
50	[−0.7, 6.0]
100	[2.9, 11.2]
200	[5.0, 13.8]

The change in MAPD for different spatial standard deviations with $\lambda_i = 10$ mm as reference is shown.

Supplementary Table II. Effect of spatial variables and median filter on MAPD.

Cartesian coordinates	Distance to surface	Median filter	95% confidence interval for change in MAPD (HU)
•	•	•	–
		•	[5.1, 15.0]
	•	•	[3.4, 12.2]
•		•	[−1.5, 1.7]
•	•		[3.1, 11.1]

The change in MAPD for several combinations of the spatial variables and the median filter is shown. The model with both types of spatial variables in combination with the median filter is used as reference.

Appendix

Algorithmic differences to previous work

In Gaussian mixture regression the joint distribution of all variables included in the model are described by a weighted sum of multivariate Gaussian distributions

$$f_Z^{\mathrm{mix}}(\mathbf{Z}) = \sum_{i=1}^{N} a_i G(\mathbf{z}; \mu_i, \Sigma_i) \quad (1)$$

where $\mathbf{Z}$ is the stochastic vector of included variables (image intensities in the different images) with observations $\mathbf{z}$. Each Gaussian in the Gaussian mixture is described by its mean value, $\boldsymbol{\mu}_i$, and covariance matrix, Σ_i. The weights α_i together with $\boldsymbol{\mu}_i$ and Σ_i form the set of parameters for the Gaussian mixture model. Typically, these parameters are estimated from a set of training data using the expectation maximization (EM) algorithm [1]. In the case of Gaussian mixture regression, a prediction for one of the variables is given by the conditional expectation of that variable given a set of observations on all of or a subset of the remaining variables [2,3].

EM regularization

As each GMM component represents a combination of tissue and location a larger number of components will be needed in this model compared to when only MR intensity variables are included. In our previous publications 20 Gaussian components were used as this is roughly the number of discernible tissue classes in the head. In the present work the number of components was increased to 50. Selecting the number of components is challenging. A low number limits the model's ability to contain all the available information in the underlying dataset, and a too large number of components make the model parameter estimation ill-conditioned.

To mitigate the estimation problem with the larger number of components, the EM algorithm was regularized by limiting the smallest singular value of the covariance matrices. This requirement was enforced each iteration. The size of the smallest singular value was selected by estimating the noise in the images. For the MR images and their filtered siblings the noise was estimated as the standard deviation of the intensities of the voxels in the air surrounding the head. For the spatial variables the standard deviation was arbitrarily set to 10 mm. Thus, with the estimated noise standard deviation, λ_i, for image i in the ith diagonal entry of Δ the regularization of a covariance matrix, Σ, is given by

$$\Lambda^{-1} \sum \Lambda^{-1} = USU^{\mathrm{T}} \tag{2}$$

$$(S_{\mathrm{reg}})_{ii} = \begin{cases} s_{ii}, & s_{ii} \geq 1 \\ 1, & s_{ii} < 1 \end{cases} \tag{3}$$

$$\sum\nolimits_{\mathrm{reg}} = \Lambda U S_{\mathrm{reg}} U \Lambda \tag{4}$$

where USU^{T} is the singular value decomposition of the left hand side of Equation 2.

The λ_i for the spatial variables need to be sufficiently large to avoid singularities but not so large as to smear the underlying distribution. The effect of λ_i on the MAPD is small at 10 mm and below as seen in Supplementary Table I. However, if the λ_i is increased above several centimetres the MAPD increases.

Number of components

While 50 Gaussians components were selected for this study the improvement of the MAPD above a few tens of components (Supplementary Figure 1) is small. While a lower number than 50 could be motivated by Supplementary Figure 1, selecting the number of components from repeated s-CT calculations would invalidate the cross-validation procedure.

Median filter

A median filter was applied to the s-CT produced by the GMR model. This reduces the salt and pepper noise that results from the poor contrast to noise ratio (CNR) for bone and interfaces compared to soft tissues. Also, the filter simplifies the determination of the external patient contour generated as a part of the dose calculation procedure at our radiotherapy department. As an additional benefit the filter improves the MAPD for the s-CT (Supplementary Table II). Given the 1.33 mm voxel size in the MR images, a required resolution of about 3 mm for brain PET attenuation maps and the 2.5 mm slice thickness of the radiotherapy dose planning CT used in this work, the s-CT resolution after filtering should be sufficient for attenuation correction and dose planning.

Spatial variables

The MAPD reduces if all spatial variables are removed (Supplementary Table II). If only the distance to surface variable is removed from the model there is no significant change in the MAPD. However, removing the Cartesian coordinates lead to an increase in the MAPD and we therefore conclude that the distance to surface could be removed from the model without deteriorating the s-CT.

References

[1] Sung HG. Gaussian mixture regression and classification. PhD thesis. Houston, Texas: Rice University; 2004.

[2] Johansson A, Karlsson M, Nyholm T. CT substitute derived from MRI sequences with ultrashort echo time. Med Phys 2011;38:2708.

[3] Johansson A, Karlsson M, Yu J, Asklund T, Nyholm T. Voxel-wise uncertainty in CT substitute derived from MRI. Med Phys 2012;39:3283–90.