

Supplementary material for Leibfarth S, et al. A strategy for multimodal deformable image registration to integrate PET/MR into radiotherapy treatment planning, Acta Oncologica, 2013;52:1353–1359.

Appendix

Quantitative assessment of registration accuracy

Several measures for the determination of registration accuracy were implemented using ITK and VTK (Visualization Toolkit, www.vtk.org). Measures based on CT and MR as well as a measure derived from the PET images were defined.

Several anatomical structures that were both visible on CT and MR were segmented automatically if possible or manually otherwise, yielding volumes C and M , respectively. These structures were skin, left and right carotid, and parts of the respiratory tract. For all volumes C and M , polygonal surface meshes \mathcal{C} and \mathcal{M} were extracted using the marching cubes algorithm [23]. Resulting \mathcal{C} were transformed to the coordinate system defined by the MR with the transform obtained by registration, yielding $\tilde{\mathcal{C}}$, from which the corresponding volume \tilde{C} was derived. For each pair of corresponding structures, the Dice similarity index (DSI) was calculated as

$$\text{DSI}(\tilde{C}, M) = \frac{2|\tilde{C} \cap M|}{|\tilde{C}| + |M|}$$

Moreover, also mean distance measures were defined. For both skin and respiratory tract, mean volume distances (MVD) were calculated as:

$$\text{MVD}(\tilde{C}, M) = \frac{1}{2} \left(\frac{1}{N_C} \sum_{i=1}^{N_C} d(\tilde{c}_i, M) + \frac{1}{N_M} \sum_{i=1}^{N_M} d(m_i, \tilde{C}) \right),$$

where \tilde{c}_i (m_i) and N_C (N_M) are the spatial center of mesh element i and the total number of mesh elements contained in \tilde{C} (M), respectively, and $d(\mathbf{p}, \mathcal{S})$ is the shortest distance of point \mathbf{p}_i to the polygonal surface mesh \mathcal{S} .

For the carotid volumes C and M , lines \mathcal{L}^C and \mathcal{L}^M defining the axial centre of the structures were extracted and \mathcal{L}^C was transformed according to the registration result, yielding $\tilde{\mathcal{L}}^C$. For each slice i in the original MR containing both a point \tilde{c}_i from $\tilde{\mathcal{L}}^C$ and m_i from \mathcal{L}^M , the Euclidean distance $d(\tilde{c}_i, m_i)$ was calculated and the mean line distance (MLD) was obtained as:

$$\text{MLD}(\tilde{\mathcal{L}}^C, \mathcal{L}^M) = \frac{1}{N_{LP}} \sum_{i=1}^{N_{LP}} d(\tilde{c}_i, m_i)$$

where N_{LP} is the total number of valid slices.

In addition, the bony structures were segmented from the CT as well as the spinal canal from the MR image. For these two structures, the non-overlapping fraction (NOF) was determined:

$$\text{NOF}(\tilde{C}, M) = 1 - \frac{|\tilde{C} \cap M|}{|M|},$$

where \tilde{C} is the transformed volume of the bones segmented from the CT and M is the volume of the spinal canal segmented from the MR.

Anatomical landmarks were defined on basis of the CT and the MR by two experienced radiation oncologists, yielding landmarks $\{\mathbf{c}_i\}_{i=1}^{N_{AL}}$ and $\{\mathbf{m}_i\}_{i=1}^{N_{AL}}$. The mean number of available landmarks per patient was $N_{AL} = 7.5$ (range 4–10). For corresponding pairs of landmarks, the mean point distance (MPD) after registration was evaluated:

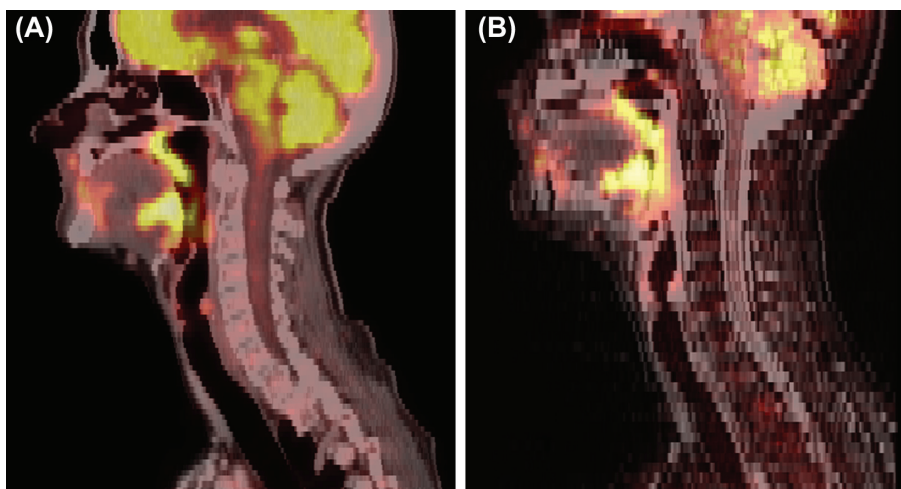
$$\text{MPD}(\{\tilde{\mathbf{c}}_i\}_{i=1}^{N_{AL}}, \{\mathbf{m}_i\}_{i=1}^{N_{AL}}) = \frac{1}{N_{AL}} \sum_{i=1}^{N_{AL}} d(\tilde{\mathbf{c}}_i, \mathbf{m}_i).$$

An additional measure was introduced to quantify the registration accuracy in the tumor region. For this region, a validation of the local registration accuracy is difficult based on the image information from CT and MR, since the intra-tumor region can be of low contrast in these imaging modalities. However, the additional PET images available in this study provide local information in this region. Therefore, the main tumor volume was derived from the PET intensities in the PET/CT (I_{PC}) using a threshold based segmentation method. The resulting volume was expanded by a margin of 7 mm, yielding the final volume Ω_T . In this volume, the normalized cross correlation (NCC) of I_{PC} and the transformed PET of the PET/MR (\tilde{I}_{PM}) was calculated:

$$\text{NCC}(I_{PC}, \tilde{I}_{PM}) = \sum_{\mathbf{x}_i \in \Omega_T} \frac{(I_{PC}(\mathbf{x}_i) - \overline{I_{PC}})(\tilde{I}_{PM}(\mathbf{x}_i) - \overline{\tilde{I}_{PM}})}{\sqrt{\sum_{\mathbf{x}_i \in \Omega_T} (I_{PC}(\mathbf{x}_i) - \overline{I_{PC}})^2 \sum_{\mathbf{x}_i \in \Omega_T} (\tilde{I}_{PM}(\mathbf{x}_i) - \overline{\tilde{I}_{PM}})^2}}$$

The NCC ranges from 0 to 1, where 0 means that the images are totally uncorrelated, and 1 that there is a perfect positive linear correlation. In the case of

a high local registration accuracy of CT and MR, and thus also of the PET images, the NCC is expected to have a value close to 1.



Supplementary Figure 1. Dataset of Patient 1. (A) PET/CT, (B) PET/MR.

Supplementary Table I. Patient characteristics.

Patient #	Age	Tumor localization	TNM	GTV volume [cm ³]
Patient 1	57	Oropharynx	cT3 cN2c M0	110.3
Patient 2	70	Hypopharynx	cT4 cN2b cM0	52.4
Patient 3	62	Hypopharynx	cT4 cN2c M0	89.0
Patient 4	64	Oropharynx	cT4 cN2c M0	89.0
Patient 5	53	Oropharynx	cT3 cN2c M0	104.0
Patient 6	44	Cervical lymph node	rcN2b M0	361.1
Patient 7	57	Oropharynx	cT2 cN2b M0	30.7
Patient 8	63	Mandibula	cT2 cN0 cM0	23.2

Supplementary Table II. Parameters used in the multi-resolution approach of DR.

Parameter	GMI	GMI+ BEP	LMI+ BEP
B-spline grid spacing (mm)	60/30/15	60/30/15	60/30/15
# iterations	5000	5000	5000
# samples	10000	10000	10000
# histogram bins	60	60	60
λ	–	250	50
L_{sub} (mm)	–	–	40

The last three parameters were optimized with regard to the registration quality measures derived from anatomical segmentations as described in *Material and methods*. If only one value is given, this value was used in all resolution levels. For GMI+ BEP and LMI+ BEP different optimal values for λ were determined. For GMI+ BEP, $\lambda = 250$ yielded better quantitative results than $\lambda = 50$, for which unrealistic deformations were observed for some of the patients.