Rectal Tumor Registration based on Virtual Templates

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***Abstract*—Rectal cancer is the second most common form of cancer in developed countries. The decision of an appropriate therapeutic approach like radiation therapy or surgical intervention largely depends on the quality of structural and functional imaging methods. Dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) is a widely accepted method for the non-invasive assessment of rectal tumors, suffering from artifacts due to bowel movement, respiratory motion and rectal coil movement. Giving the fact that MRI contrast media change the signal intensities over time, classical image registration strategies fail. To overcome these problems, the algorithm Virtual Template Registration (VTR), originally designed for the registration of DCE-MRI Renography, is adapted to register DCE-MRI data from rectal tumors. VTR derives a smooth virtual template image series from the DCE-MRI data, where motion artifacts are minimized but intensity changes due to contrast media uptake are preserved. The original dynamic time series (source images) is then registered by applying elastic registration to the generated virtual template. Our results indicate, that motion artifacts, visible in evaluated time courses, are significantly reduced and allow for a more differentiated analysis of different rectal tumor types.**

I. Introduction

Colorectal cancer is the second most common form of cancer in developed countries. In 1998, there were 131,000 new cases of colorectal cancer and 56,000 deaths from colorectal cancer in the United States [1], [2].

Detailed anatomic information on tumor extent is essential to plan surgical procedures and to identify patients who may benefit from radiotherapy [3], [4]. In comparison to endorectal ultrasound, MRI is able to visualizes not only the intestinal wall but also the surrounding pelvic anatomy [5], suggesting MRI as the preferable imaging method. DCE-MRI is an attractive technique for assessing the vascular physiology of tumors, by combining good anatomical details because of its high-contrast spatial resolution and a large field of view with the ability to quantify vascular parameters [6], [7], [8]. Limitations of rectal MRI image quality are given by artifacts due to bowel movement, respiratory motion and the movement of the rectal coil, which can impair diagnostic studies [9], [10].

Several algorithms, dealing with DCE-MRI motion correction, have been presented within the last years [11], [12], [13], [14], [15], [16], [17], [18]. However, all these methods suffer from the following major problems:

First, the signal enhancement induced by the uptake of contrast media is temporally varying and second, the identification of appropriate template images for the registration of the dynamic time series is difficult because anatomical structures may arise in postcontrast images [19]. To overcome these problems an image registration procedure named Virtual Template Registration (VTR) [20], originally developed to register DCE-MRI Renography datasets, was adapted. The major idea of VTR is to derive a virtual template image series (template images) from the underlying signal time course in every voxel. This leads to motion free template images that still include uptake information of contrast media. The source images are finally registered to the generated template images. In this work we demonstrate that creating template images overcome the problem of intensity changes due to the uptake of contrast media and reduces motion artifacts to a high extent. This allows for a more differentiated analysis of the time-courses in different tumor tissues, which is needed to plan further surgical or radiotherapy procedures.

II. Methods

To focus on the area of the rectal tumor, a region-of-interest (ROI) with the size of 64x64 pixels was marked manually within the first frame of the source images. The same ROI was then applied to all source images.

A. Preprocessing and template image generation

The original images were preprocessed by applying a total variation based smoothing algorithm (TV-L2, ROF) [21], [22] to all images of the DCE time series to reduce the influence of noise and fine scale details which are not needed for generating the template images. To achieve the same denoising results over all source images the same TV regularization parameters where used. The parameters where set empirically by visual inspection (number of iterations = 70, λ = 0.015).

The choice of an appropriate template image for the registration of contrast enhanced dynamic series is not trivial because of intensity changes varying with time (Fig. 1). The idea of VTR is not to take only one template image for the registration process, but rather to generate template images corresponding with each source image. The main advantages of this template sequence is that motion artifacts between two

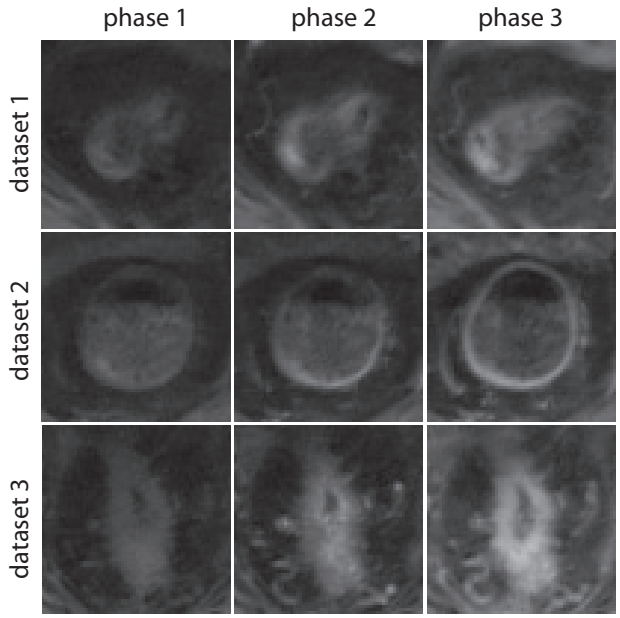

Fig. 1. Three DCE-MRI datasets of rectal tumors shown at three characteristic phases: pre-contrast (column 1), begin of contrast-enhancement (column 2), contrast-enhanced (column 3).

consecutive images are decreased but intensity changes within an image due to the uptake of contrast media are kept (Fig. 2). This is done by filtering each pixel over the time domain separately by using a regularized Tikhonov filtering algorithm [14], [15]. This purely temporal regularization results in a second dynamic time series where each image is used as a template image for the non-rigid registration algorithm (Fig. 3). Each image of the original dataset is finally registered to its corresponding virtual template dataset. For visual assessment of the registration result, checkerboard composite images are created. This is done by taking small alternate blocks from the image before and after registration which are finally combined following a checkerboard pattern (Fig. 6).

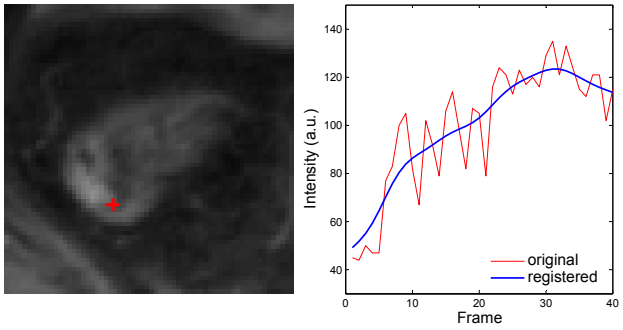

Fig. 2. Temporal smoothing of the red marked pixel in the left image over the time domain (40 images) by using regularized Tikhonov filtering.

B. Image registration

A non-rigid (elastic) registration algorithm [23] accounts for the elastic nature of the characteristic motion and was applied to register each of the images from the dynamic time series with its corresponding image from the template image time series. The algorithm was performed iteratively including the following steps:

VTR: Virtual Template Registration

1. Denoise the input images $I(x,t)$ to obtain $I_p(x,t)$ by applying a TV based smoothing algorithm

$$I_p(x,t) = \int_\Omega |\nabla I_p(x,t)|\, d\Omega + \frac{1}{2\lambda}\int_\Omega (I_p(x,t) - I(x,t))^2 d\Omega \tag{1}$$

where x represents the spatial and t the temporal domain.

2. Initialize the images $I_r(x,t) = I_p(x,t)$ and repeat the following until changes in $I_r(x,t)$ are less than a given tolerance:

3. Compute the template sequence $I_s(x,t)$ by using a regularized Tikhonov filtering algorithm

$$J_x(I) = \int_0^T \left[|I(t) - I_p(x,t)|^2 + |I'(t)|^2\right] dt \tag{2}$$

for each fixed x and setting $I_s(x,t) = I(t)$.

4. Compute the new registered sequence $I_r(x,t)$ by minimizing the functional

$$J_t(u) = SSD(I_p, I_s, u) + R_{elas}(u) \tag{3}$$

where u denotes the vector-valued displacement field. SSD and R_{elas} are defined as follows

$$SSD(I_p, I_s, u) = \int_\Omega |I_p(x + u(x), t) - I_s(x,t)|^2 dx \tag{4}$$

$$R_{elas}(u) = \int_\Omega \left[\lambda|\nabla \cdot u(x)|^2 + \mu/2|\nabla u(x)^T + \nabla u(x)|^2\right] dx \tag{5}$$

for each fixed t and setting $I_r(x,t) = I_p(x + u(x), t)$. μ and λ are the Lamé Constants used for elastic registration [23] and where set empirically by visual inspection. The term $|\nabla u(x)^T + \nabla u(x)|^2$ in (5) penalizes the departure from rigidity.

C. Imaging protocol

In vivo DCE-MRI data were obtained from routine examinations on a 1.5T MRI scanner (Siemens Symphony). A 3D FLASH sequence was used (FOV/TR/TE/α=300mm/3.34ms/1.10ms/15°), image matrix of 256x256, slice thickness of 4.0mm and a temporal resolution of 6.53s at 40 time points.

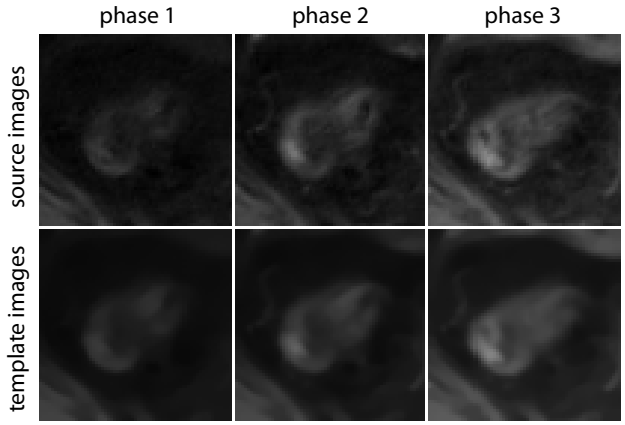

Fig. 3. Source images (first row) compared to their generated template images (second row) after the first iteration of VTR. Three different images from the whole dynamic time series (40 images) are shown.

D. Motion evaluation

The actual displacement of the tumor is measured in the horizontal direction [24]. Therefore the distance from a defined reference point at the border of the tumer to the left border of the image is calculated (Fig. 4). This reference line gives a quantitative parameter to score and evaluate the displacement before and after applying VTR.

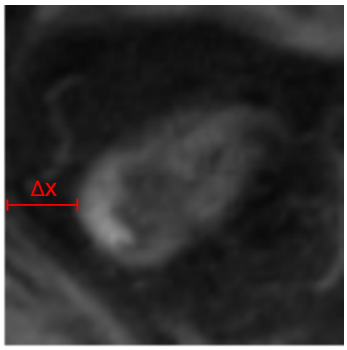

Fig. 4. Reference line to measure the actual displacement Δx of the tumor.

III. Results

By investigating the generated template images, it is seen that motion is already reduced but intensity changes according to the uptake of contrast media are still present (Fig. 3). The performance of the proposed VTR algorithm to register dynamic rectal tumor data was evaluated using *in-vivo* DCE-MRI data. Five different datasets of different patients were investigated where motion and perfusion results were observed before and after registration. The same set of parameters was used for all datasets. The average motion of the investigated datasets ranges from 3-5 pixels (Fig. 4). After applying VTR, the average motion could be decreased to 0-2 pixels. Fig. 5 shows the registration results in terms of absolute difference images for two consecutive images of the original dynamic time series and for the registered data set. The performance of

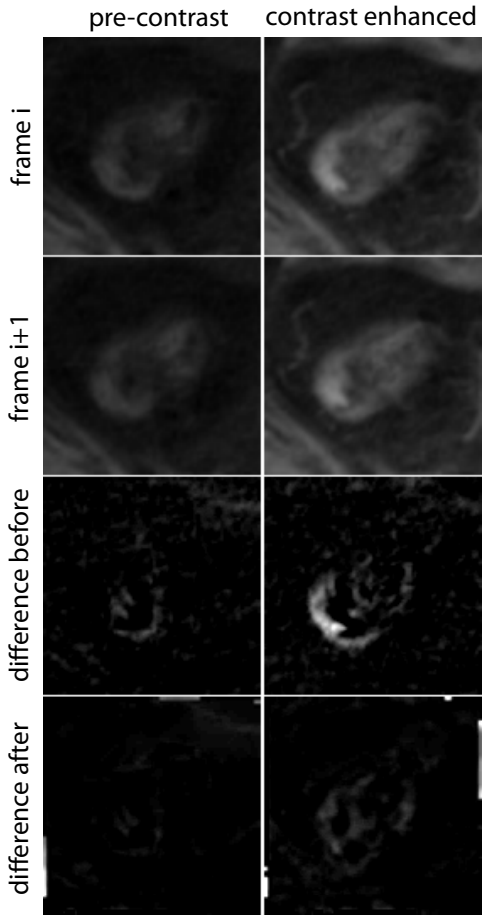

Fig. 5. Absolute difference images of one patient dataset at two different stages. The first column represents the registration result during the pre-contrast stage, the second column during the contrast enhanced stage. Images in the first and second row show two consecutive images, the third row represents difference images without registration, the last row represents difference images after applying VTR.

the proposed algorithm during the contrast-enhancement stage is seen in Fig. 6 where results in the presence of contrast media before and after registration are shown in two different patient datasets where spatial displacement is marked by white arrows.

Fig. 7 represents the effect of VTR on the time domain. Displacements of the rectal tumors for unregistered and registered dynamic time series are shown. Critical regions near the borders of the tumors are investigated before and after applying VTR. Since the low frequency trend is maintained while the high frequency perturbations are damped, it is seen that motion artifacts are obviously decreased while the uptake characteristics of the contrast media is preserved.

IV. Discussion and Conclusion

Image registration in the presence of intensity changes is a well-studied topic in computer vision. Several similarity measures for intermodal registration, that are robust to contrast changes, e.g. mutual information (MI) or correlation ratio (CR), have been developed so far. When dealing with DCE-

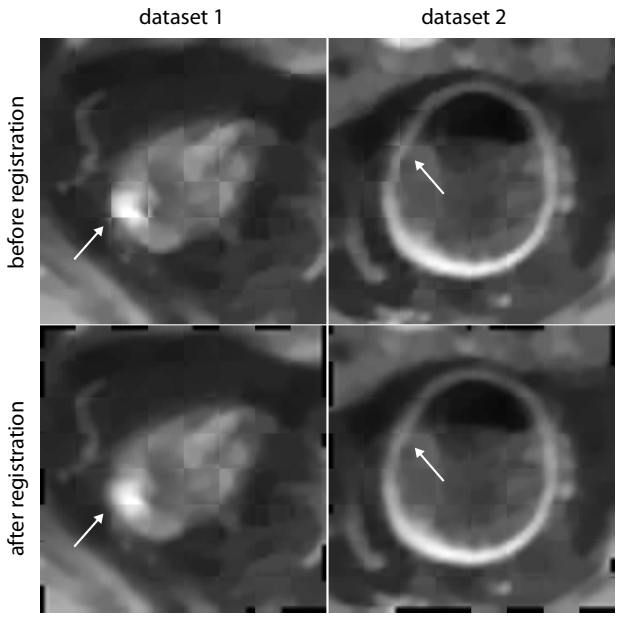

Fig. 6. Checkerboard composite images of two consecutive frames during the contrast-enhancement stage for four different datasets before and after applying VTR.

MRI motion correction, it is difficult to distinguish between intensity changes due to motion or due to contrast media uptake. For this reason, registration is particularly critical during the contrast enhancement stage. Due to the uptake of contrast media, anatomical structures may arise in post-contrast images that were not present in the pre-contrast images [19]. These new image features may cause conventional registration methods using intensity-based similarity metrics to fail as shown for example in registration using MI for pre- vs. postcontrast MRI images of focal breast lesions where artifactual deformations in regions of contrast enhancement have been observed [19], [25], [26]. Commonly, the movement artifacts between subsequent images are determined [13] which leads to the problem of error propagation along the dynamic series if the previous registration result is used as input for the next. This also can be inconvenient since the movements between two frames can be very large, depending on the time resolution of the dataset.

In this work an algorithm named Virtual Template Registration (VTR), originally designed for minimizing motion artifacts in DCE-MRI Renography, is adapted and evaluated to rectal tumor registration. After applying VTR to different datasets, it is obvious, that the displacement of the rectal tumors could be recovered as well as the characteristics of the signal enhancement in the tumors (Fig. 7). By investigating the checkerboard images (Fig. 6), the effect of VTR is seen clearly especially near border regions of the tumors.

The strength of the algorithm is its ability to accommodate strong and fast intensity changes related to the uptake of contrast media. VTR leads to good registration results in rectal tumors which is important for further investigations to allow for a better differentiation of perfusion in different tissue types.

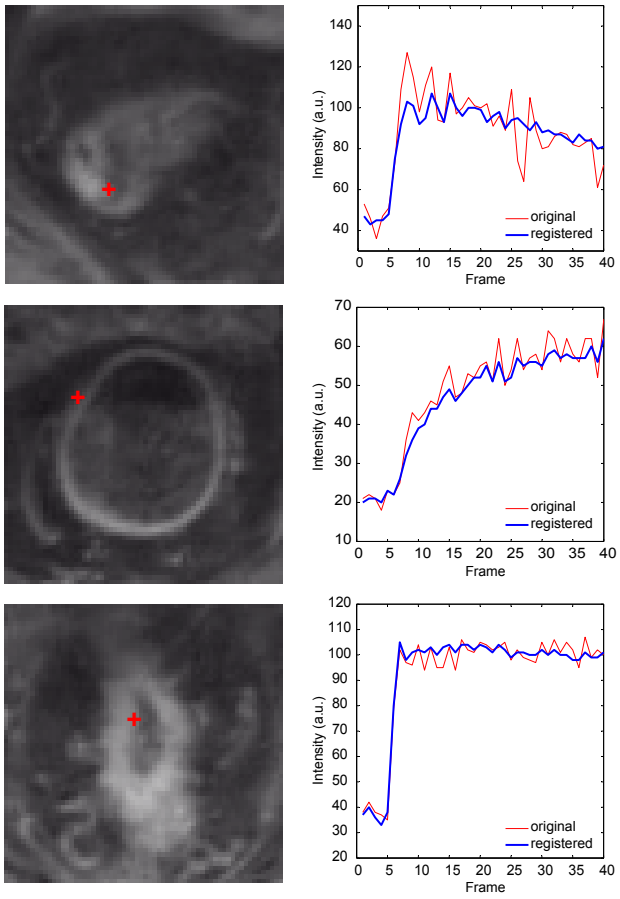

Fig. 7. Results after applying VTR to the whole DCE-MRI series. Three datasets are investigated, where the registered dynamic time series is compared to the original (non-registered) dynamic time series.

Future studies will be performed to evaluate the impact of the proposed method to different functional parameters.

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References

[1] D. M. Eddy. Screening for colorectal cancer. *Ann Intern Med*, 113(5):373–384, Sep 1990.

[2] Ahmedin Jemal, Rebecca Siegel, Jiaquan Xu, and Elizabeth Ward. Cancer statistics, 2010. *CA Cancer J Clin*, 60(5):277–300, 2010.

[3] R. G. Beets-Tan, G. L. Beets, A. C. Borstlap, T. K. Oei, T. M. Teune, M. F. von Meyenfeldt, and J. M. van Engelshoven. Preoperative assessment of local tumor extent in advanced rectal cancer: CT or high-resolution MRI? *Abdom Imaging*, 25(5):533–541, 2000.

[4] P. Quirke, P. Durdey, M. F. Dixon, and N. S. Williams. Local recurrence of rectal adenocarcinoma due to inadequate surgical resection. histopathological study of lateral tumour spread and surgical excision. *Lancet*, 2(8514):996–999, Nov 1986.

[5] Christian Klessen, Patrik Rogalla, and Matthias Taupitz. Local staging of rectal cancer: the current role of MRI. *Eur Radiol*, 17(2):379–389, Feb 2007.

[6] Vicky Goh, Anwar R Padhani, and Shahnawaz Rasheed. Functional imaging of colorectal cancer angiogenesis. *Lancet Oncol*, 8(3):245–255, Mar 2007.

[7] Franco Iafrate, Andrea Laghi, Pasquale Paolantonio, Marco Rengo, Paolo Mercantini, Mario Ferri, Vincenzo Ziparo, and Roberto Passariello. Preoperative staging of rectal cancer with MR Imaging: correlation with surgical and histopathologic findings. *Radiographics*, 26(3):701–714, 2006.

[8] MS Juchems and AJ Aschoff. Aktuelle Bildgebung beim Rektumkarzinom. *Chirurg*, Mar 13, 2009.

[9] Juergen Scheidler. Staging of Rectal Cancer using Multislice-CT and MR Imaging. 2002.

[10] Xiao Ming Zhang, Hong Lei Zhang, Dexin Yu, Yong Dai, Dongsong Bi, Martin R Prince, and Chuanfu Li. 3-T MRI of rectal carcinoma: preoperative diagnosis, staging, and planning of sphincter-sparing surgery. *AJR Am J Roentgenol*, 190(5):1271–1278, May 2008.

[11] Ying Sun, Marie pierre Jolly, and Jos M. F. Moura. Integrated registration of dynamic renal perfusion MR images. *Proceedings of IEEE International Conference on Image Processing*, pages 1923–1926, 2004.

[12] Peter J. Yim, Hani B. Marcos, Peter L. Choyke, Matthew McAuliffe, Delia McGarry, and Ian Heaton. *Registration of Time-Series Contrast Enhanced Magnetic Resonance Images for Renography*. CBMS '01. IEEE Computer Society, Washington, DC, USA, 2001.

[13] E. L. Giele, J. A. de Priester, J. A. Blom, J. A. den Boer, J. M. van Engelshoven, A. Hasman, and M. Geerlings. Movement correction of the kidney in dynamic MRI scans using FFT phase difference movement detection. *J Magn Reson Imaging*, 14(6):741–749, Dec 2001.

[14] G. Gerig, R. Kikinis, W. Kuoni, G. K. von Schulthess, and O. Kbler. Semiautomated ROI analysis in dynamic MR studies. Part I: Image analysis tools for automatic correction of organ displacements. *J Comput Assist Tomogr*, 15(5):725–732, 1991.

[15] R. P. Woods, S. R. Cherry, and J. C. Mazziotta. Rapid automated algorithm for aligning and reslicing PET images. *J Comput Assist Tomogr*, 16(4):620–633, 1992.

[16] Dwarikanath Mahapatra and Ying Sun. Nonrigid registration of dynamic renal MR images using a saliency based MRF model. *Med Image Comput Comput Assist Interv*, 11(Pt 1):771–779, 2008.

[17] Giovanni A Buonaccorsi, Caleb Roberts, Sue Cheung, Yvonne Watson, James P B O'Connor, Karen Davies, Alan Jackson, Gordon C Jayson, and Geoff J M Parker. Comparison of the performance of tracer kinetic model-driven registration for dynamic contrast enhanced MRI using different models of contrast enhancement. *Acad Radiol*, 13(9):1112–1123, Sep 2006.

[18] A. Melbourne, D. Atkinson, M. J. White, D. Collins, M. Leach, and D. Hawkes. Registration of dynamic contrast-enhanced MRI using a progressive principal component registration (PPCR). *Phys Med Biol*, 52(17):5147–5156, Sep 2007.

[19] Giovanni A Buonaccorsi, James P B O'Connor, Angela Caunce, Caleb Roberts, Sue Cheung, Yvonne Watson, Karen Davies, Lynn Hope, Alan Jackson, Gordon C Jayson, and Geoffrey J M Parker. Tracer kinetic model-driven registration for dynamic contrast-enhanced MRI time-series data. *Magn Reson Med*, 58(5):1010–1019, Nov 2007.

[20] M. Hofer, S. Keeling, G. Reishofer, M. Riccabona, M. Aschauer, and R. Stollberger. DCE-MRI Non-Rigid Kidney Registration. *Proc. Intl. Soc. Mag. Reson. Med. 18*, 18:3054, 2010.

[21] Leonid I. Rudin, Stanley Osher, and Emad Fatemi. Nonlinear total variation based noise removal algorithms. *Phys. D*, 60:259–268, November 1992.

[22] Antonin Chambolle. An algorithm for total variation minimization and applications. *Journal of Mathematical Imaging and Vision*, 20:89–97, 2004.

[23] Jan Modersitzky. *Numerical Methods for Image Registration*. Number ISBN 978 019 852841 8. Oxford University Press, 2004.

[24] Florian Lietzmann, Frank G. Zoellner, Henrik J. Michaely, and Lothar R. Schad. Untersuchung von selbstnavigierenden MR-Sequenzen fr die Perfusionsbildgebung der Nieren. *Zeitschrift fuer Medizinische Physik*, 20(2):124 – 133, 2010. Kidney imaging.

[25] C. Tanner, J. Schnabel, D. Chung, M. Clarkson, D. Rueckert, D. Hill, and D. Hawkes. Volume and Shape Preservation of Enhancing Lesions when Applying Non-rigid Registration to a Time Series of Contrast Enhancing MR Breast Images. 1935:CH371–CH371, 2000.

[26] C. Tanner, J. Schnabel, A. Degenhard, A. Castellano-Smith, C. Hayes, M. Leach, D. Hose, D. Hill, and D. Hawkes. Validation of Volume-Preserving Non-rigid Registration: Application to Contrast-Enhanced MR-Mammography. 2488:307–314, 2002.