LCC Demons with Divergence Term for Liver MRI Motion Correction

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ABSTRACT

Contrast-enhanced liver MR image sequences acquired at multiple times before and after contrast administration have been shown to be critically important for the diagnosis and monitoring of liver tumors and may be used for the quantification of liver inflammation and fibrosis. However, over multiple acquisitions, the liver moves and deforms due to patient and respiratory motion. In order to analyze contrast agent uptake one first needs to correct for liver motion. In this paper we present a method for the motion correction of dynamic contrast-enhanced liver MR images. For this purpose we use a modified version of the Local Correlation Coefficient (LCC) Demons non-rigid registration method. Since the liver is nearly incompressible its displacement field has small divergence. For this reason we add a divergence term to the energy that is minimized in the LCC Demons method. We applied the method to four sequences of contrast-enhanced liver MR images. Each sequence had a pre-contrast scan and seven post-contrast scans. For each post-contrast scan we corrected for the liver motion relative to the pre-contrast scan. Quantitative evaluation showed that the proposed method improved the liver alignment relative to the non-corrected and translation-corrected scans and visual inspection showed no visible misalignment of the motion corrected contrast-enhanced scans and pre-contrast scan.

Keywords: Liver Contrast-enhanced MRI, Non-parametric image registration, Motion correction, Local Correlation Coefficient (LCC) Demons, Incompressibility, Divergence

1. INTRODUCTION

Contrast-enhanced liver MR image sequences have become critical to diagnosis of liver tumors, monitoring of therapy, and may be useful for the quantification of liver inflammation and fibrosis. However, over multiple acquisitions after contrast administration the liver moves and deforms between image acquisitions due to the patient and respiratory motion. In order to analyze the contrast agent uptake one first needs to correct for liver motion. A typical approach for liver image correction of changes due to motion is to register the post-contrast scans to the pre-contrast scan. In addition to the accuracy, the execution time of the motion correction is an important factor since post-contrast liver MR image sequences typically have several scans and the motion correction needs to be completed within minutes for the approach to be clinically useful. Parametric non-rigid registration methods, e.g. the ones using various types of splines to represent the spatial transformation, typically take hours to register sequences of several 3D scans and for this reason are too slow for clinically practical liver motion correction. On the other hand, the Demons non-parametric registration method[1] is significantly faster. The intensity of post-contrast liver scans is increased relative to the intensity of the pre-contrast liver scan due to the contrast uptake and for this reason we use Local Correlation Coefficient (LCC) Demons introduced by Cachier and Pennec (2000).[2] The liver is nearly incompressible due to a high percentage of water[3] and consequently its displacement field has small divergence. For this reason we add a divergence term to the energy that is minimized by the LCC Demons method.

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2. METHODS

2.1 Sum of Squared Difference (SSD) based Demons

The variational formulation of the Demons method[1] was introduced by Modersitzki,[4]

$$E_1 = \frac{1}{2}\int_{\Omega} \frac{(S(x-u(x)) - M(x))^2}{\|\nabla S(x)\|^2 + \alpha^2 k^2}\, d\vec{x}\ , \forall \vec{x} \in \Omega \tag{1}$$

where S is the static image, M the floating image, $k = M - S$, and $\vec{u}$ the displacement field. Parameter α, which is not present in the original Demons formulation, was introduced by Cachier *et al.*[5] and it was termed a homogenization factor. The purpose of α is to control the maximal displacement, which is bounded by $\frac{1}{2\alpha}$.[5] From the Euler-Lagrange equations one can obtain

$$\vec{u} = (S - M)\frac{\vec{\nabla} S}{\left\|\vec{\nabla} S\right\|^2 + \alpha^2 k^2} \tag{2}$$

2.2 Local Correlation Coefficients (LCC) based Demons

The Demons algorithm is based on the assumption that the intensity at corresponding locations of the two images is the same. In the case of contrast-enhanced liver MR image sequences this assumption is not valid since the image intensity is changed due to the uptake of the contrast agent. For this reason we use the LCC Demons introduced by Cachier and Pennec (2000).[2] The sum of local correlation coefficients over the image domain is utilized as the image similarity measure and it is defined as:

$$SLCC(S, M) = \sum_{p \in N^n} LCC_p(S, M), \tag{3}$$

where

$$LCC_p(S, M) = \frac{\langle S, M \rangle_p}{\sigma_p(S)\sigma_p(M)}, \tag{4}$$

$$\sigma_p^2(S) = \overline{S^2}_p - \overline{S}_p^2 = G_{\sigma_{LCC}} * (S^2)[p] - (G_{\sigma_{LCC}} * S)^2[p], \tag{5}$$

$$\begin{aligned} \langle S, M \rangle_p &= \overline{SM}_p - \overline{S}_p \overline{M}_p & (6)\\ &= G_{\sigma_{LCC}} * (SM)[p] - (G_{\sigma_{LCC}} * S)[p](G_{\sigma_{LCC}} * M)[p], & (7) \end{aligned}$$

and G_σ is the Gaussian smoothing filter with standard deviation σ,

$$G_\sigma(\vec{r}) = \frac{1}{\left(\sqrt{2\pi}\sigma\right)^3} e^{\frac{\|\vec{r}\|^2}{2\sigma^2}}. \tag{8}$$

The local correlation coefficient $LCC_p(S, M)$ is centered at p and its computation involves convolutions with the Gaussian kernel G, which provides isotropic weighted averaging and can be applied, due to its separability, as successive convolutions with one-dimensional Gaussian kernels, which speeds up the execution.

Expression (2) can be rearranged as

$$\vec{u} = \frac{-2H\vec{\nabla} H}{\left\|\vec{\nabla} H\right\|^2 + 4\alpha^2 (H)^2} \tag{9}$$

where $H = (S(x - u(x)) - M(x))^2$. In the case of LCC demons one can use $H = LCC(S(x - u(x)), M(x))$ and change the sign in front of the expression to account for the fact that SSD needs to be minimized and LCC maximized. The energy gradient is

$$\frac{\partial SLCC(S, M)}{\partial u_p} \approx \frac{1}{\sigma_p(S)\sigma_p(M)} \left((S - \overline{S}_p) - (M - \overline{M}_p)\frac{< S, M >_p}{\sigma_p^2(M)} \right) \vec{\nabla} M \tag{10}$$

This is a simplified energy gradient expression without Gaussian convolutions to speed up the computations.[2]

2.3 Divergence term

It can be shown that the Jacobian of a smooth spatial transformation can be approximated as

$$J \approx 1 + \nabla \cdot \vec{u}, \tag{11}$$

where $\vec{u}$ is the displacement field.[6] For nearly incompressible materials $J \approx 1$, from which it follows that the divergence of the displacement field, $\nabla \cdot \vec{u}$, is small. Since the liver is nearly incompressible[3] we add the following term

$$\int_{\Omega} (\nabla \cdot \vec{u})^2 \ d\vec{x}. \tag{12}$$

to the total energy that is minimized. The minimization of this term results in displacement fields with small divergence, i.e. in spatial transformations that are nearly volume-preserving.

2.4 Final algorithm

We look for the displacement field $\vec{u}$ that minimizes

$$E = SLCC + \frac{\lambda}{2} \int_{\Omega} (\nabla \cdot \vec{u})^2 \ d\vec{x}, \tag{13}$$

where parameter λ controls the relative importance of the two terms. To minimize E one can update the displacement field in the following way,

$$u_n \leftarrow G_{\sigma_{diffusion}} * \left\{ u_n + G_{\sigma_{fluid}} * \left[\frac{2LCC\vec{\nabla}SLCC}{\left\| \vec{\nabla}SLCC \right\|^2 + 4\alpha^2 (LCC)^2} + \lambda \sum_{l=1}^{3} \frac{\partial^2 u_l}{\partial x_l \partial x_n} \right] \right\} \ , n \in \{1, 2, 3\}, \tag{14}$$

where G_σ is given by (8). The application of the inner Gaussian filter (with σ_{fluid}) results in fluid-like regularization and the application of the outer Gaussian filter (with $\sigma_{diffusion}$) results in diffusion-like regularization.[7] After updating the displacement field the floating image is updated,

$$M(\vec{r}) \leftarrow M\left(\vec{r} + \vec{u}(\vec{r})\right). \tag{15}$$

The steps given by (14) and (15) are iterated until SLCC, given by (3), no longer improves. After that we run 3 more iterations, which helps avoid local maxima, and we set the maximal number of iterations to 150.

By experimenting we have found the following as the optimal parameter values: $\alpha = 0.5$, $\lambda = 10$, $\sigma_{LCC} = 3mm$, $\sigma_{fluid} = 5mm$ and $\sigma_{diffusion} = 4mm$. We used these parameter values for all the subjects and the following size of the discrete 1D Gaussian kernel,

$$N = \left\lceil \frac{8 * \sigma}{\delta} \right\rceil, \tag{16}$$

where δ is the voxel size in millimeters and $\lceil x \rceil = \text{ceil}(x)$ is the smallest integer not less than x.

2.5 Rigid and non-rigid liver motion

Clifford et al.[8] reported liver movement of 12∼26 mm in the cranio-caudal direction, 1∼12 mm in the anterior-posterior direction and 1∼3 mm in the lateral direction and the error introduced by assuming rigid liver motion of 3 mm on average was explained as non-rigid (tissue) deformation. Since the maximal liver movement was over 10 mm according to these studies, direct non-rigid registration would require longer computational times and possibly would have problems to completely align the pre- and post-contrast scans. For this reason we first perform translation-only registration to remove the global liver motion and then apply the non-rigid registration method described in Section 2.4 to correct for tissue deformation.

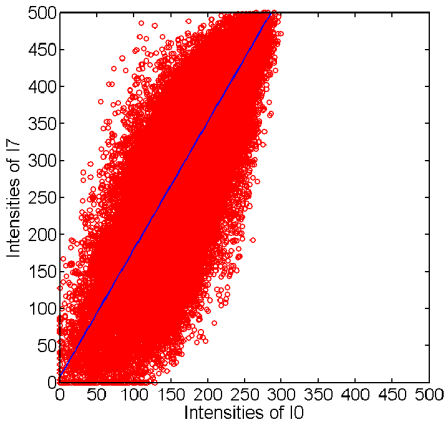


Figure 1. The intensity relation between the pre-contrast and a post-contrast scan is shown for a representative case. The blue line represents a least-squares affine fit to the data.

3. RESULTS

3.1 MR scans and subjects

Contrast enhanced MRI has been utilized to detect the presence of liver inflammation in acute and chronic liver disease. We applied the proposed motion-correction technique to our clinically routine liver contrast enhanced MRI for four randomly selected consecutive subjects, two healthy volunteers and two patients. Each subject image series had a pre-contrast scan and seven post-contrast scans. For each post-contrast scan we corrected for the liver motion relative to the pre-contrast scan. Each scan had 128 contiguous slices with 256 x 256 pixels, the in-plane resolution of 1.4648 mm and the slice thickness of 3 mm.

The intensity relation between pre-contrast scan and a contrast enhanced scan is shown in Figure 1 for a representative case. The intensity relationship can be approximated with an affine model. The standard Demons method, which assumes identical image intensities, fails to properly register pre- and post-contrast scans due to the approximately affine intensity relationship. For this reason we used the LCC Demons method, which was designed to register images with locally affine intensity relationship.

3.1.1 Checkerboard display

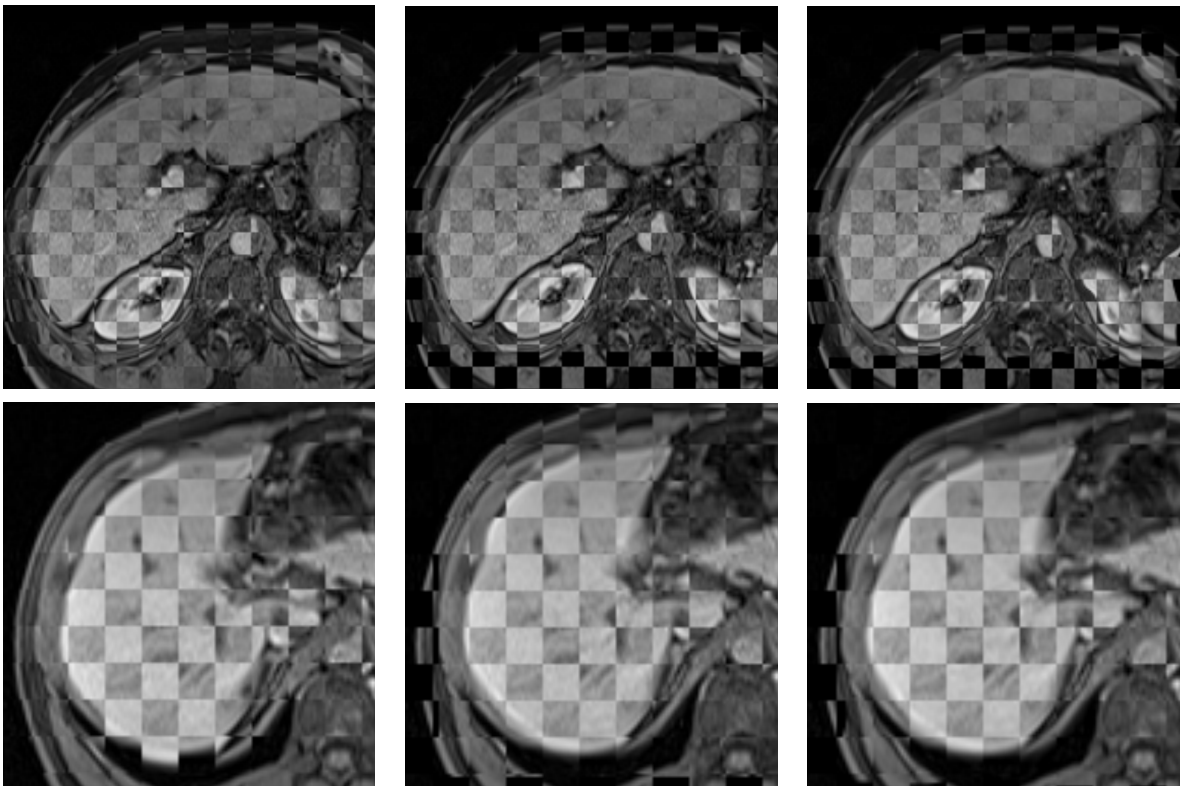
Figure 2 shows checkerboard displays of non-registered images, after translation-only registration and after the registration with the proposed method. Checkerboard display is a visualization technique for inspection of image registration that shows alternate squares from the two images. While the translation-only registration removes most of the misalignment it cannot account for liver deformation, which is recovered by the proposed method.

3.1.2 Image alignment quantification

To quantify the improvement in the alignment we calculated the normalized cross correlation (NCC) between the pre-contrast scan and all the scans in the sequence of contrast enhanced scans for each subject. Tables 1 and 2 show NCC values for the non-registered scans, after translation-only registration and after the registration by the proposed method for the image sequences of the four subjects. Note that for all the scans the translation-only registration improves the alignment (in the sense of the NCC value) relative to the non-registered images, which is further improved by the proposed method.

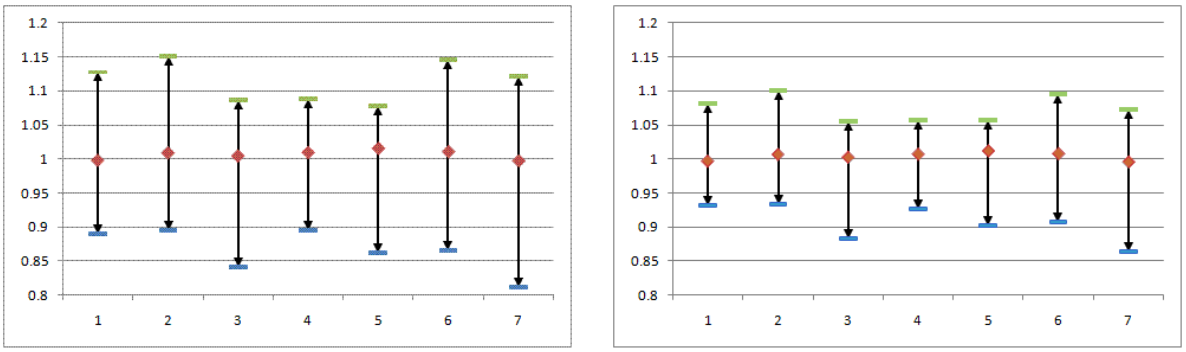
3.1.3 Jacobian measures

The determinant of the Jacobian matrix of the transformation (denoted as J) represents the relative change of local volume. If $J < 1$ the local volume compresses, if $J > 1$ the local volume expands and if $J = 1$ the local volume remains the same. In general soft tissues are nearly incompressible due to their high percentage of water, which is almost perfectly incompressible. The liver was also reported as being nearly incompressible.[3,9] As it was explained in Sec. 2.3, near incompressibility corresponds to small divergence of the displacement field. To



(a) (b) (c)

Figure 2. Checkerboard displays of a slice of the pre-contrast and post-contrast scan with no registration (a), translation-only registration (b), and registration with the proposed method (c) are shown for one subject in the first row and for another subject in the second row. Note the misalignment of the liver boundary in (a), partial alignment in (b) and full alignment of (c).



LCC Demons LCC Demons with the divergence term

Figure 3. The maximum, minimum and mean value of the Jacobian for the seven scan sequence of a representative case are shown for LCC Demons (left) and LCC Demons with the divergence term (right). The red diamond denotes the mean value, the blue bar the minimal value and the green bar the maximal Jacobian value. Note that the Jacobian values are consistently closer to 1 for the LCC Demons with the divergence term, indicating better modeling of the near incompressibility.

inspect the effect of adding the divergence term to the energy we compared the minimal, mean, and maximal Jacobian values between LCC Demons and LCC Demons with the divergence term. Figure 3 shows Jacobian

values for the two methods for a representative case. LCC Demons with the divergence term resulted in Jacobian values consistently closer to 1, with the deviation from 1 ranging from -10% to $+7\%$ as opposed to the case of LCC Demons that had the deviation from 1 ranging from -14% to $+11\%$. Parameter λ controls the relative importance of the divergence and SLLC terms. The larger λ the more important the divergence term, which translates to better modeling of the near incompressibility of the liver. However, there is a trade off since the larger λ the less effect the image similarity (SLCC term) has on the result, which may result in suboptimal image alignment. For all the cases we used $\lambda = 10$.

3.2 Rigid and non-rigid components of the liver motion

In our study with four subjects the rigid motion of the liver accounted for $1.4\ mm - 7.0\ mm$ shift in the anterior-posterior direction, $1.4\ mm - 5.6\ mm$ in the lateral direction and $3.0\ mm - 9.0\ mm$ in the cranio-caudal direction. The non-rigid component of the liver motion was $1.1\ mm - 3.0\ mm$ on average and its maximal value was $2.7\ mm - 5.6\ mm$. Details of the rigid and nonrigid components of the liver motion for the seven scans for each of the four subjects are given in Tables 1 and 2.

3.3 Computational performance

On average it took about 2 min to complete the translation-only registration and 28 min to complete the registration by the proposed method between a pair of scans using Matlab on a Duo core CPU running at 2.4 GHz. Therefore to register a complete sequence consisted of a pre-contrast scan and 7 contrast-enhanced scans on average it took 3 hr and 30 min. As shown in Figure 4, 99% of image matching was completed in the first 100 iterations based on the NCC measure. Therefore, one can save $\frac{1}{3}$ of the computational time for the non-rigid registration, i.e. reduce 28 min to 19 min for a pair of scans or 3 hr and 30 min to 2 hr and 45 min for the 7 scan sequence.

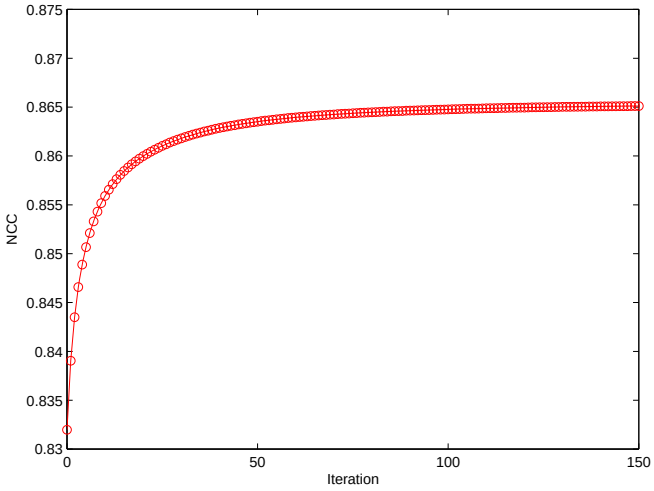


Figure 4. NCC vs. iterations for a representative case

4. CONCLUSION

We based our liver motion correction approach on the Demons method because of its speed compared to other nonrigid registration methods. Due to the contrast agent uptake the image intensities increase from the pre-contrast to post-contrast scans and therefore we used LCC Demons method since it is designed to register images with non-identical intensities. The standard Demons method does not impose any constraints on the displacement field other than its smoothness; rather it is purely driven by the image information. Since the liver is nearly incompressible its displacement field has small divergence. For this reason, we added a term in the LCC Demons method that keeps the divergence of the recovered displacement field small, i.e. the transformation close to volume-preserving. The addition of the near-incompressibility of the liver to the registration method helps

Subject 1	Scan 1	Scan 2	Scan 3	Scan 4	Scan 5	Scan 6	Scan 7
NCC (NR)	0.814	0.814	0.883	0.908	0.888	0.887	0.862
NCC (TO)	0.833	0.878	0.896	0.913	0.911	0.892	0.904
NCC (PM)	0.865	0.902	0.934	0.945	0.943	0.937	0.939
RD (A)	0	1.4	0	0	1.4	0	1.4
RD (L)	1.4	1.4	1.4	1.4	0	0	0
RD (C)	3	3	3	3	3	3	3
MEAND	1.544	1.097	1.825	1.497	1.576	1.879	1.439
MAXD	3.053	2.720	4.855	3.639	3.255	3.694	3.676
MEANJ	0.997	1.007	1.003	1.008	1.012	1.009	0.996
STDJ	0.014	0.021	0.016	0.014	0.017	0.018	0.019
MAXJ	1.081	1.100	1.056	1.057	1.058	1.095	1.073
MINJ	0.932	0.933	0.884	0.927	0.902	0.907	0.864
Subject 2	**Scan 1**	**Scan 2**	**Scan 3**	**Scan 4**	**Scan 5**	**Scan 6**	**Scan 7**
NCC (NR)	0.739	0.855	0.634	0.657	0.797	0.828	0.618
NCC (TO)	0.741	0.873	0.841	0.848	0.887	0.898	0.828
NCC (PM)	0.870	0.893	0.898	0.910	0.933	0.936	0.898
RD (A)	1.4	1.4	5.6	4.2	2.8	2.8	7.0
RD (L)	0	0	1.4	1.4	0	1.4	1.4
RD (C)	3	0	9	9	6	3	9
MEAND	2.304	0.977	1.975	2.214	2.441	1.681	2.874
MAXD	4.246	2.984	5.027	4.968	5.232	3.494	5.614
MEANJ	0.982	1.003	1.011	1.013	1.011	1.019	1.009
STDJ	0.022	0.019	0.023	0.022	0.018	0.017	0.023
MAXJ	1.073	1.070	1.112	1.103	1.071	1.103	1.124
MINJ	0.837	0.932	0.905	0.898	0.916	0.932	0.889

Table 1. Numerical results for two healthy volunteers (subjects 1 and 2). The abbreviations in the table are defined as: Normalized Cross Correlation (NCC) for the case of no registration (NR), translation-only registration (TO) and registration by the proposed method (PM), Rigid Displacement (RD) A (Anterior-Posterior), L (Lateral), C (Cranio-Caudal), Mean of Displacement (MEAND), Max of Displacement (MAXD), Mean of Jacobian determinant (MEANJ), Standard deviation of Jacobian determinant (STDJ), Maximum of Jacobian determinant (MAXJ) and Minimum of Jacobian determinant (MINJ). Displacements are expressed in mm.

correct for its motion despite the presence of noise, image artifacts and regions with weak image features. The method was tested on sequences of eight 3D liver MRI scans of four subjects, each composed of a pre-contrast scan and seven contrast-enhanced scans. The resulting motion corrected contrast-enhanced scans showed no visible misalignment with the pre-contrast scans. In this study, the average liver deformation was $1.1\ mm - 3.0\ mm$ while the maximal liver deformation was $2.7\ mm - 5.6\ mm$. The current Matlab implementation took on average 2 hr and 45 min to correct for the motion of a 7 scan sequences. We expect that the processing time may be reduced to a few minutes if the method is implemented using graphics hardware, which would make the proposed methodology practical for routine clinical use.

5. ORIGINALITY

The work presented in this paper is original and has not been submitted to any other conference or journal for consideration.

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Subject 3	**Scan 1**	**Scan 2**	**Scan 3**	**Scan 4**	**Scan 5**	**Scan 6**	**Scan 7**
NCC (NR)	0.598	0.657	0.595	0.647	0.622	0.628	0.578
NCC (TO)	0.718	0.772	0.728	0.741	0.777	0.776	0.743
NCC (PM)	0.826	0.867	0.855	0.843	0.893	0.890	0.858
RD (A)	4.2	4.2	5.6	2.8	4.2	5.6	5.6
RD (L)	4.2	5.6	5.6	5.6	4.2	5.6	4.2
RD (C)	0	0	0	0	0	0	3
MEAND	2.823	2.581	2.713	2.502	2.697	2.979	2.936
MAXD	5.593	4.985	5.322	5.363	5.203	5.493	5.104
MEANJ	1.024	1.005	1.011	1.020	1.018	1.020	1.020
STDJ	0.024	0.023	0.031	0.024	0.020	0.020	0.023
MAXJ	1.120	1.108	1.115	1.097	1.098	1.123	1.114
MINJ	0.946	0.926	0.897	0.918	0.921	0.936	0.938
Subject 4	**Scan 1**	**Scan 2**	**Scan 3**	**Scan 4**	**Scan 5**	**Scan 6**	**Scan 7**
NCC (NR)	0.703	0.805	0.800	0.805	0.850	0.772	0.768
NCC (TO)	0.732	0.805	0.836	0.832	0.858	0.838	0.841
NCC (PM)	0.795	0.849	0.863	0.874	0.900	0.881	0.880
RD (A)	4.2	1.4	1.4	1.4	1.4	2.8	2.8
RD (L)	0	0	0	1.4	1.4	1.4	0
RD (C)	0	0	3	0	0	3	3
MEAND	1.880	1.489	1.740	1.058	1.094	1.704	1.255
MAXD	5.096	3.668	3.346	3.272	2.699	3.746	2.890
MEANJ	1.015	1.014	1.006	1.010	1.011	1.010	1.008
STDJ	0.019	0.015	0.016	0.017	0.014	0.018	0.019
MAXJ	1.105	1.077	1.091	1.080	1.095	1.164	1.148
MINJ	0.940	0.950	0.927	0.928	0.932	0.927	0.910

Table 2. Numerical results for two patients (subjects 3 and 4). The abbreviations in the table are defined as: Normalized Cross Correlation (NCC) for the case of no registration (NR), translation-only registration (TO) and registration by the proposed method (PM), Rigid Displacement (RD) A (Anterior-Posterior), L (Lateral), C (Cranio-Caudal), Mean of Displacement (MEAND), Max of Displacement (MAXD), Mean of Jacobian determinant (MEANJ), Standard deviation of Jacobian determinant (STDJ), Maximum of Jacobian determinant (MAXJ) and Minimum of Jacobian determinant (MINJ). Displacements are expressed in mm.

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