Simultaneous Registration and Bias Correction of Brain Intra-operative MR Images

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ABSTRACT

Intra-operative MR imaging is an emerging tool for image guided (neuro)surgery. Due to the small size of the magnets and the short acquisition time, the images produced by such devices are often subject to distortions. In this work, we show the particular case of images provided by an ODIN device (Odin Medical Technologies, Newton, MA 02458, USA). Such images suffer from geometric distortions and an important bias field in the luminance. In order to simultaneously correct these deformations, we propose to register a preoperative ODIN image with a diagnosis MR high resolution image while compensating the bias field.

Keywords: Intra-operative images, multi-modal signal processing, MR intensity correction.

1. INTRODUCTION

In order to perform robust rigid or non-rigid registration, robust similarity measures have to be defined. This measures must be able to catch complex dependencies between multi-modal signals such as a Magnetic Resonance (MR) and Positron Emission Tomography (PET). Viola,[1] Maes and Collignon[2] propose to use Mutual Information (MI) as registration criterion.
However MI is no more than a divergence measure on the marginal histograms and on the joint distribution of the gray levels of the source and target images. Therefore the registration can fail if one of these images suffer from *spatially* variant luminance distortions. Mutual Information based registration is obviously able to deal with uniform luminance bias. For this reason, it is important to examine robust ways to correct luminance deformations before or while performing the registration.

Different approaches can be followed to correct the bias field in the gray levels of the intra-operative image. First, a model of the luminance distortions must be chosen and inverted. Secondly, to optimize the parameters of this model, an optimization strategy must be defined.

If no other information is available, a first possibility consists of achieving the correction using the biased image itself because luminance distortions introduce disruptions in the statistical distribution of the image. Of course, the correction strategy is easier if an *a priori* model on the marginal distribution of the unbiased image is available. Van Leemput[3] *et all* introduced Gaussian assumptions about the distribution of each *class* in the input image. This leads to simultaneous classification and bias correction.

In the context of intra-operative image acquisition, a first *diagnosis* MR image is acquired before surgery. To calibrate the intra-operative device, a second image acquisition is performed in the operating room before surgery. Because of the small size of the magnets and the short acquisition time, the images produced by such devices are often subject to luminance distortions, and are characterized by a limited field of view and low spatial resolution. Therefore, it would be interesting to perform a registration between the two modalities. Since registration can fail if one of the two images is biased,[4] it is convenient to examine simultaneous registration and bias correction algorithms. The resulting bias correction will be based on the pre-operative unbiased MR image.

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This paper is organized as follows. The first section describes a polynomial bias correction model as it was introduced by Likar[5] along with different criterions to optimize the parameters of this model. A simultaneous registration and bias correction algorithm (such as previously described in[4]) is introduced in section 3. In section 4 the method is first validated on a typical example and the results are then discussed. Finally, section 5 summarizes the conclusions and gives a brief survey about future work.

2. MARGINAL BIAS CORRECTION

2.1. Bias correction model

In our implementation, we used the model developed by Likar[5] to correct the distortions in the intra-operative image. It is assumed that it is possible to get an unbiased version $U(\vec{x})$ of the biased luminance $N(\vec{x})$ with multiplicative and additive corrections

$$U(\vec{x}) = M(\vec{x}) \cdot N(\vec{x}) + A(\vec{x}) \tag{1}$$

The additive and multiplicative bias corrections consist of a weighted polynomial basis functions sums.

$$A(\vec{x}) = \sum_i a_i A_i(\vec{x}) = \sum_i a_i \frac{P_i(\vec{x}) - a_{ni}}{a_{ei}} \tag{2}$$

$$M(\vec{x}) = 1 + \sum_i m_i M_i(\vec{x}) = 1 + \sum_i m_i \frac{P_i(\vec{x}) - m_{ni}}{m_{ei}} \tag{3}$$

where $P_i(\vec{x})$ is a polynom with degree lower than a fixed order.

The coefficients noted by a_{ei} and m_{ei} normalize a_i and m_i to get coefficients evolving in the same dynamic. This is particularly useful while optimizing. The role of a_{ni} and m_{ni} coefficients is to keep the mean of the luminance function. This is made to guarantee a certain *stability* to the transform. More concretely, it can be written by the following conditions (N_Ω refers to the number of voxels in the input image)(see Likar[5] for more details)

- the *mean preserving* condition :

$$1/N_\Omega \cdot \sum_{\vec{x} \in \Omega} U(\vec{x}) = 1/N_\Omega \cdot \sum_{\vec{x} \in \Omega} N(\vec{x}) \tag{4}$$

- and *parameters normalization* conditions :

$$\begin{aligned} 1/N_\Omega \cdot \sum_{\vec{x} \in \Omega} |N(\vec{x}) \cdot M_i(\vec{x})| &= 1 \\ 1/N_\Omega \cdot \sum_{\vec{x} \in \Omega} |A_i(\vec{x})| &= 1 \end{aligned} \tag{5}$$

The mean preserving condition (4) can be rewritten as

$$1/N_\Omega \sum_i \left[\sum_\Omega m_i N(\vec{x}) \frac{P_i(\vec{x}) - m_{ni}}{m_{ei}} + \sum_\Omega a_i \frac{P_i(\vec{x}) - a_{ni}}{a_{ei}} \right] = 0 \tag{6}$$

To get mean preserving and normalization coefficients independent from m_i and a_i, a possible choice is to take

$$\sum_\Omega N(\vec{x})(P_i(\vec{x}) - m_{ni}) = 0 \quad \forall i \tag{7}$$

and

$$\sum_\Omega (P_i(\vec{x}) - a_{ni}) = 0 \quad \forall i \tag{8}$$

This leads to a really simple expression

$$m_{ni} = \frac{\sum_\Omega N(\vec{x})P_i(\vec{x})}{\sum_\Omega N(\vec{x})} \tag{9}$$

and

$$a_{ni} = \frac{1}{N_\Omega}\sum_\Omega P_i(\vec{x}) \tag{10}$$

It can be shown[6] that the same conditions leads to

$$m_{ei} = \begin{cases} \frac{1}{N_\Omega}\sum_\Omega(N(\vec{x})(P_i(\vec{x}) - m_{ni})) & \text{if } M_i(\vec{x}) > 0 \\ \frac{1}{N_\Omega}\sum_\Omega(N(\vec{x})(m_{ni} - P_i(\vec{x}))) & \text{if } M_i(\vec{x}) > 0 \end{cases} \tag{11}$$

$$a_{ei} = \begin{cases} \frac{1}{N_\Omega}\sum_\Omega(P_i(\vec{x}) - m_{ni}) & \text{if } M_i(\vec{x}) > 0 \\ \frac{1}{N_\Omega}\sum_\Omega(m_{ni} - P_i(\vec{x})) & \text{if } M_i(\vec{x}) > 0 \end{cases} \tag{12}$$

2.2. Optimization criterion

In former section, a bias correction model was introduced. The best a_i and m_i coefficients have now to be chosen by optimizing an appropriate criterion. In the following, we show how a simple criterion derives from a Maximum Likelihood (ML) approach.
If a bias correction vector C contains the a_i and m_i parameters, and $\vec{y}$ is defined as a vector containing the gray values y_i of all the pixels in the input image, the best bias correction will be found by a classical ML approach

$$C_{opt} = \arg\max_C \log(p(\vec{y}|C)) \tag{13}$$

where p denote the estimated probability density function using a classical estimation technique (histogram, Kernel Estimation,...).

It is now assumed that all the voxel intensities are statistically independent.[3] The probability density distribution of the image $\vec{y}$ for a given model becomes

$$p(\vec{y}|C) = \prod_i p(y_i|C) \tag{14}$$

Injecting (14) in (13) leads to the maximization of

$$\sum_{i=1}^{N_\Omega} \log(p(y_i|C)) \tag{15}$$

The sum in (15) provides (with an N_Ω factor) an estimation of $\mathrm{E}\{\log(p(y_i|C))\}$. It is now obvious that maximizing (15) is equivalent to minimizing the marginal entropy of the $\vec{y}$ image given the model C defined by

$$H(\vec{y}) = -\mathrm{E}\{\log(p(\vec{y}|C))\} \tag{16}$$

This leads naturally to the conclusion that the bias field produces a dispersion in the probability distribution of the input image. The use of marginal entropy as criterion to correct this dispersion is an efficient (but radical) way to compensate the bias. Of course, the assumption that all voxel intensities were independent is not really satisfied... To take into account the dependence between intensities of adjacent pixels, other criterions can be introduced. For example, it is possible to use conditional entropy between voxel values and their neighbor.[6] Such strategy avoids divergence in the optimization process (minimizing entropy can lead to change the density probability function into a Dirac delta function !).
Another optimization strategy is the use of conditional entropy between the voxel intensities and the gradient norm of the input image. The gradient takes into account dependencies between a voxel and its neighbor. There is thus sense to use it as an *a priori* knowledge(see Solanas[6] fore more details).

3. REGISTRATION AND BIAS

3.1. Optimization Criterion

As described in section 2.2, a possible bias correction strategy is the minimization of the marginal entropy in the input image. In the intra-operative (ODIN) case, another approach could be using the unbiased preoperative image as a reference to correct the bias.
Instead of marginal entropy, the criterion to optimize becomes a robust similarity measure between the pre- and intra-operative images. It remains now to determine the most suitable criterion. The theory developed by Butz[4] about multi-modal signal processing introduces a general framework about robust similarity measures. If X and Y are the features (luminance, norm of luminance gradient, ...) extracted from the source and target image, a class of similarity measures can be derived from the general expression

$$e_n(X,Y) = \frac{I(X,Y)^n}{H(X,Y)^{1-n}} \quad \text{with}\, n \in [0,1] \tag{17}$$
$$\text{where} \quad MI(X,Y) = H(X) + H(Y) - H(X,Y)$$

In (17), $H(X,Y)$ represent the Joint Entropy between features X and Y. The Mutual Information between X and Y is noted by $I(X,Y)$. Both Joint Entropy and Mutual Information are estimated using a joint histogram between random variables X and Y.
It can be observed that equation (17) summarizes different well known similarity measures used in image registration.

1. If $n = 0$, maximizing (17) is equivalent to minimizing the Joint Entropy between X and Y. Because $H(X,Y) \geq H(X)$ and $H(X,Y) \geq H(Y)$, this approach consist of selecting *efficient* features (i.e. features with low entropy). This is similar to the bias correction approach we discussed in former section.
2. If $n = 1$, maximizing (17) is equivalent to maximizing Mutual Information.
   Butz[4] shows that this approach is equivalent to minimizing a lower error bound on the probability error. Nevertheless, it has been observed (see Gil[7]) that Mutual Information will select features containing as much information as possible. This could increase needlessly the marginal entropy of selected features. If one of these features is the output of a polynomial bias correction filter, this could increase the bias instead of correcting it.
3. If $n = \frac{1}{2}$, a compromise is made between the efficiency of features ($H(X,Y)$) and the minimization of the lower error bound ($MI(X,Y)$). This criterion is equivalent to Normalized Entropy.
   In our case, it seems to be the best compromise to correct the bias and perform a registration simultaneously.

To evaluate the criterion (17), an estimation of the joint probability density between X and Y is needed. This is usually performed using joint histograms.[2] The discretization step in the histogram (i.e. the number of bins) in both axis is an important parameter to be fixed in the registration process. It can be represented by a first feature selection filter before evaluating the criterion. This filter simply consists in a first quantization of the input images in order to select the representative information in both images discarding the redundant noise. Butz[4] has shown that an optimal number of bins in both images can be selected with an adapted similarity measure. In asmuch that decreasing the number of bins obviously decreases the marginal entropies of the image representations, simply maximizing Mutual Information is dangerous and converges to the maximum number of bins (high entropy features). With a Normalized Entropy criterion, a compromise can be made between Mutual Information and low entropy characteristics. This *efficient* behavior explains why Normalized Entropy is preferred to perform a correct quantification in the modalities to register.

3.2. Bias and Affine transformations

If we note by T the spatial transform applied from ODIN image to the diagnosis image, and by P the polynomial transform applied to the gray levels of the ODIN image, the optimization objectives can be formalized as follows

$$[C^{opt}, \vec{t}^{opt}, n_x, n_y] = \arg \max_{C \in \mathrm{R}^q, \vec{t} \in \mathrm{R}^p, n_x \in \mathrm{Z}^+, n_y \in \mathrm{Z}^+} e_n\{P(O_{n_x}(X)), T^{-1}(D_{n_y}(X))\} \tag{18}$$

S_{pop}	population size	500
p_{conv}	convergence percentage for terminaison condition	0.001
n_{gen}	maximum number of generations	50
p_{mut}	mutation probability	0.5
p_{cross}	crossover probability	0.7
$p_{replace}$	proportion of chromosomes to be replaced at each generation	0.5

Table 1. Genetic Optimization parameters.

where X is an uniform Random Variable on the space domain of the ODIN image, O_{n_x} and D_{n_y} denote the luminance functions in the ODIN and diagnosis image discretized with n_x and n_y bins. During the optimization process, the transformation is applied to the diagnosis image and resized to the same domain as the ODIN image. The spatial transform is implemented in our case by a rigid transform (3 translations and 3 rotations). The polynomial transform we used is multiplicative and linear,3 m_i independent parameters have to be determined. The number of bins in both images was also optimized. The resulting number of parameters to optimize was thus set to 11. For visualization purpose, the spatial transform is inverted before being applied to the ODIN image. A global view of the algorithm is sketched in figure 1.

3.3. Optimization Method

We investigated the use of different optimization methods. Powell optimization seemed not robust enough to perform a correct registration. Moreover, these kind of optimization algorithm can not deal with a complex search domain. In our case, the number of bins (n_x and n_y) are discrete numbers whereas polynomial and rigid (translation and rotation) coefficients are real parameters. We have finally chosen a genetic algorithm and used the GALIB[8] library implementing different genetic algorithms.

The basis principle of such optimization routine consists of generating a population (whose members are called *chromosomes*) and to define an evolving strategy for this initial population. Two particular operators are defined to go from one population to the next one : crossover and mutation. In our case, a chromosome is implemented by an array containing 11 float numbers. The crossover operator generates a new chromosome from two "parents" by intertwining their genes. The mutation operator is obtained by randomly substitution of certain array elements (in the bounds of the optimization domain). A mutation probability has to be defined. We used the particular implementation of a *steady-state* algorithm. This algorithm selects at each iteration the best chromosomes. The chromosomes with a poor value of the objective function are replaced using the crossover and mutation operators. The number of chromosomes to be replaced at each generation is determined by a fixed replacement probability. This is another parameter to be fixed. The algorithm stops when a fixed convergence to the best element of the current population is reached. A maximal number of generations is also fixed to avoid excessive computation time. The particular values we used in our implementation are presented in table 1.

In our case, an acceptable initial condition is needed due to the limited field of view of the ODIN modality. It is also necessary to get reasonable computation time. The *search domain* for the genetic routine is a (10x10x10)mm box in translation centered on the initial condition. The bounds for polynomial bias correction were fixed to $[-10, 10]$ for each m_i coefficient. The values for p_{mut} and p_{cross} (c.f. table 1) are bigger than usual. An important value for p_{mut} avoids convergence to local minima because of exploring the whole *search domain*.

4. RESULTS AND DISCUSSION

The Genetic Algorithm (figure 1) simultaneously optimizes three blocks : the number of bins in the pre and intra-operative modalities, the polynomial transform parameters (bias correction) and the geometric parameters (translations and rotations). In this section, the results obtained for each block will be successively discussed.

Selecting the number of bins in both modalities allows to compare two similarity measures : Mutual Information (MI) and Normalized Entropy (NE). After optimization, the selected numbers of bins were fixed to 5 in the diagnosis image and to 10 in the ODIN image. The value of Mutual Information and Normalized Entropy is plotted in figure 2 as a function of the number of bins in the intra operative modality (keeping 5 bins in

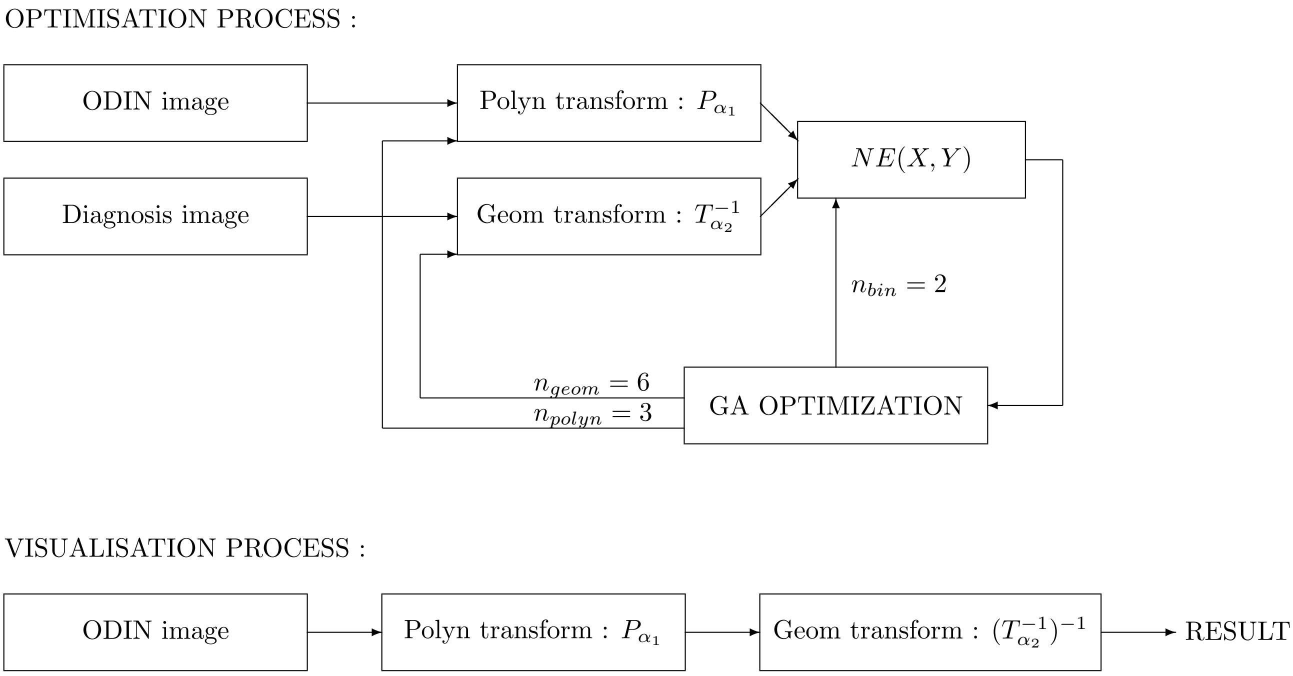

Figure 1. Our algorithm uses a genetic optimization routine to find the best parameters in order to register pre- and intra-operative modalities (6 parameters), correct the gray levels of the intra-operative image (3 parameters) and find the optimal number of bins to build the joint histogram (2 parameters). Once the algorithm has converged, we apply the luminance and the geometric transform to the intra-operative image. The similarity measure used is the Normalized Entropy between the source (diagnosis image) and the target (ODIN) image.

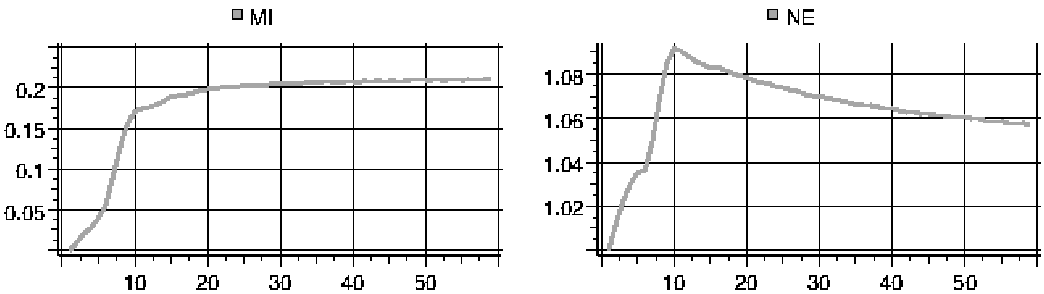

Figure 2. Selection of the numbers of bins in the ODIN image using Mutual Information (MI) or Normalized Entropy (NE). Both MI and NE presents a global optimum but MI converges to the maximum number of bins. The selection is therefore not relevant. On the contrary, NE converges to an intermediate number of bins.

the diagnosis image). It clearly appears that NE presents a maximum for 10 bins in the ODIN image. On the contrary, MI selects always the maximum number of segments and emphasizes the marginal entropy in both images.

To examine if the selected number of bins is anatomically relevant, the corresponding threshold (figure 3) is applied to both images. The quantization in the diagnosis image allocates different bins to the ventricles, the brain or the skull. Due to the noise in the intra operative image, the quantization is more confused even if the polynomial correction try to correct the bias. However, this seems enough to converge to a satisfying alignment.

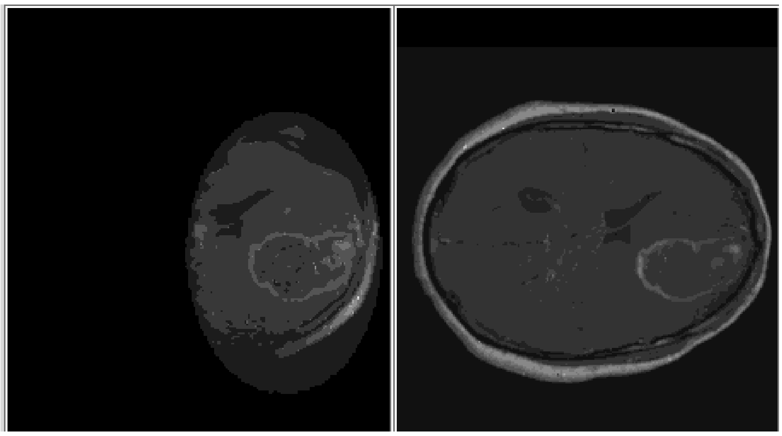

Figure 3. Optimal bins selection in both images using Normalize Entropy. Relevant objects are isolated (brain, ventricles, skull) emphazing common information between the involved modalities.

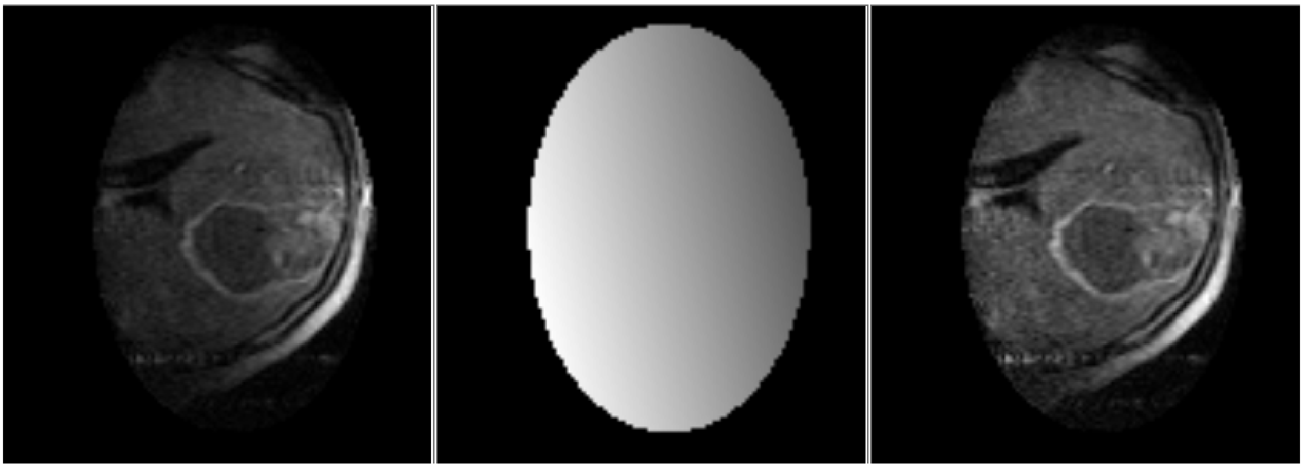

Figure 4. A view of the bias correction obtained by our algorithm. We used a multiplicative and linear correction to correct the bias in the intra-operative modality. The coefficient of the polynomial correction in the gray levels and the geometric transform parameters were obtained by maximization of a similarity measure with a standard MR image of the same patient.

Our algorithm converges to a multiplicative bias correction visible in the middle part of figure 4. It can be clearly observed that the correction emphasizes the inferior left corner. Figure 5 compares the joint histograms after simple rigid registration and after simultaneous registration and bias correction. It appears that the resulting joint histogram after simultaneous optimization strategy is more compact.

Once the polynomial and the rigid registration applied to the ODIN image, we obtained the result showed in figure 6 (the contours of the preoperative image are over-imposed to the corrected ODIN image). It can be observed that the tumor and the ventricles are well registered. However, near the boundaries of the ODIN image, geometric distortions appear. More data would be needed (for example phantom images) to evaluate the importance of these distortions.

5. CONCLUSION

In this paper, we showed the potentially large bias field of interventional MR scans can be corrected while registration. This leads to a more robust registration algorithm and satisfying bias correction. This correction

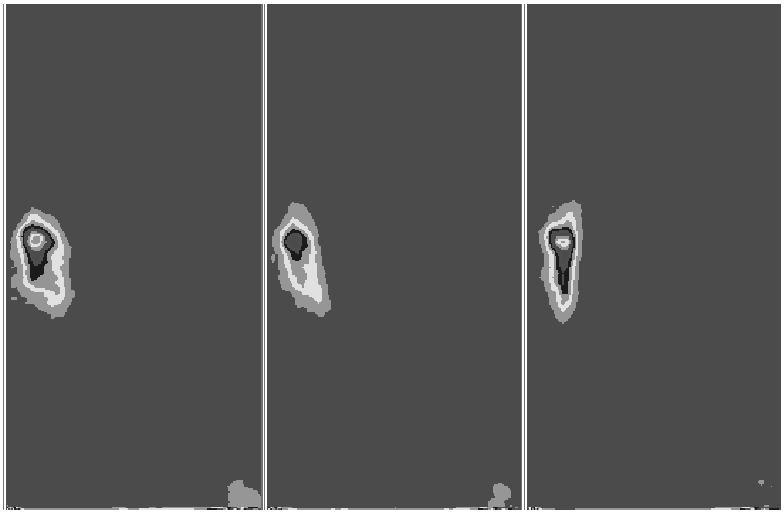

Figure 5. The first histogram we show is the initial joint histogram between the gray levels in the two images (ODIN and diagnosis MR image). The second histogram is obtained after rigid registration without bias correction. The third one is the joint histogram we get after simultaneous registration and bias correction of the ODIN and the diagnosis image. We see that in our case, the bias correction is necessary to avoid dispersion in the joint distribution.

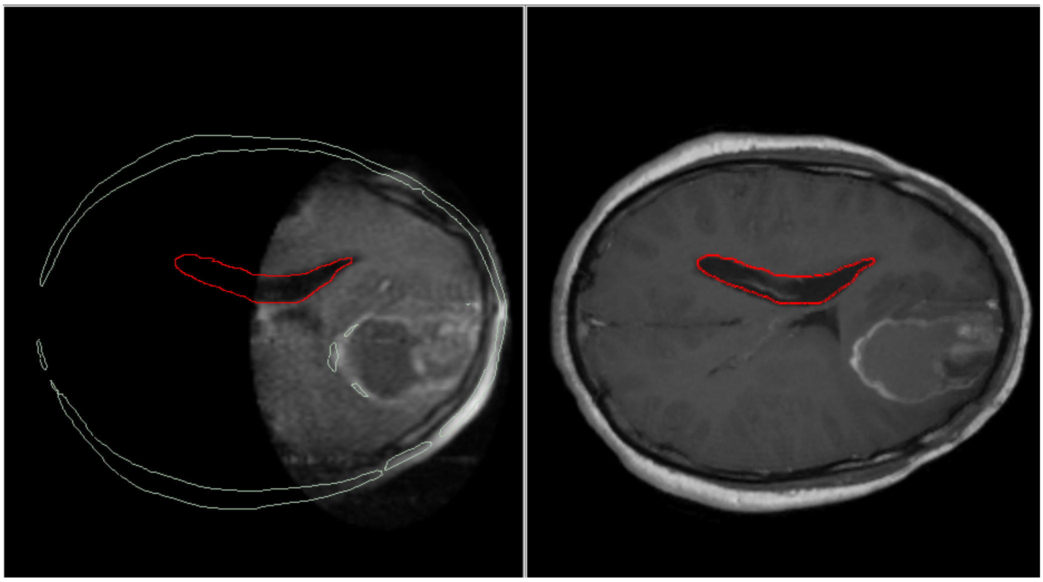

Figure 6. Registration result between the pre- and intra-operative modalities. The contours of preoperative image are reported on the intra-operative (ODIN) image.

is obtained by maximizing a similarity measure with an unbiased image which has more sense that a marginal correction without any reference to perform the bias field correction.

The number of bins in both images is an important parameter to get a correct bias correction. It can be incorporated in the optimization process if an adapted similarity measure is chosen. It has been observed that Normalized Entropy (preferentially to Mutual Information) was a suitable measure to reach this task.

As a future work, it would be interesting to improve the *spatial* transform by using more complex models such as polynomial or spline models to compensate the deformations introduced by the intra-operative images acquisition device. The advantage of such correction strategy is the immediate visual validation obtained by comparing the diagnosis MR image and the calibrated intra operative image.

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