Neurosurgery for functional disorders guided by multimodality imaging

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ABSTRACT

This paper presents a procedure for combining MR anatomical information and a stereotactic reference obtained from a CT study with a Leksell frame attached to the patient's head, in order to guide neurosurgery of functional disorders. MRI acquisition can be performed well before the surgery, without the stereotactic frame. The day of the intervention, after attaching the Leksell frame to the patient, a CT image (1.5 mm slices) is acquired. This study will provide the stereotactic reference and includes only the part of the brain where the disorder is located. Before surgery, physicians register the MRI with the CT using a procedure based on an automated algorithm (Mutual Information) and visually check the result. MRI is used to locate the target in the brain, while the frame visible in the CT allows to calculate the stereotactic 3D coordinates. Frame references are located on the MRI image allowing to calculate Leksell coordinates of any given point. When the exact position of relevant structures has been recorded, the physicians proceed with the surgery.

The protocol has been tested in ten patients, showing a positive surgical outcome with a significant decrease of the functional disorders. The method has proved to be accurate enough, avoiding the use of stereotactical frames during the MR acquisition and making the clinical procedure simpler and faster.

Keywords: MRI, CT, neurosurgery, image guided surgery, registration, functional disorders, Parkinson, stereotaxy, Mutual Information

1. INTRODUCTION AND BACKGROUND

Movement disorders in Parkinson's disease may be reduced with surgical interventions in thalamic and subthalamic areas either implanting stimulating electrodes or burning a certain area in this part of the brain [1-4]. Leksell showed the utility of the palidotomy in these patients in the 60's, but the incorporation of the treatment with levodopa reduced its indications since 1968 [1]. Limitations of this pharmacological therapy together with advances in medical imaging and image guided surgery had led to reconsider neurosurgery as an appropriate alternative for the control of parkinsonian resting tremor, reducing in some cases the secondary effects of levodopa treatment [3, 5].

In stereotactic neurosurgery, the frame designed by Leksell is attached to the patient's head in order to define a coordinate system that allows to guide the intervention identifying the target position (**Figure 1** shows a surface rendering from a CT scan of a patient with the frame attached). Two different spaces have to be registered: preoperative three-dimensional images (CT and MRI) and the patient with the attached frame in the operating room. The first one provides anatomical information to locate the target in the patient's brain, while the second one defines the stereotactic coordinates.

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Some authors have proposed the use of a CT of the patient with the head-mounted Leksell frame to locate the target. The frame reference points are visible in all the images, and from them the stereotactical coordinates can be calculated [4, 6-9]. But modern stereotactic surgery can take advantage from more advanced imaging tools, like magnetic resonance imaging (MRI). MRI provides better contrast than CT for soft tissues, improving the reliability of target determination [10]. Although neurosurgery guided only by MRI can be performed [11], MRI acquisition with the Leksell frame attached poses some technical difficulties: The use of the frame increases pre-acquisition time, since the frame references must be filled in with fluid contrast in order to make them visible in the MR images. On the other hand, clinically significant geometric distortion may be present in standard MRI images, specially at the borders of the field, thus compromising the reliability and requiring a method for correcting this artifact [12]. For these reasons, the combined use of CT for frame reference and MR for target location appears as a very good solution. This paper presents a complete procedure for image-guided neurosurgery on patients suffering from movement disorders.

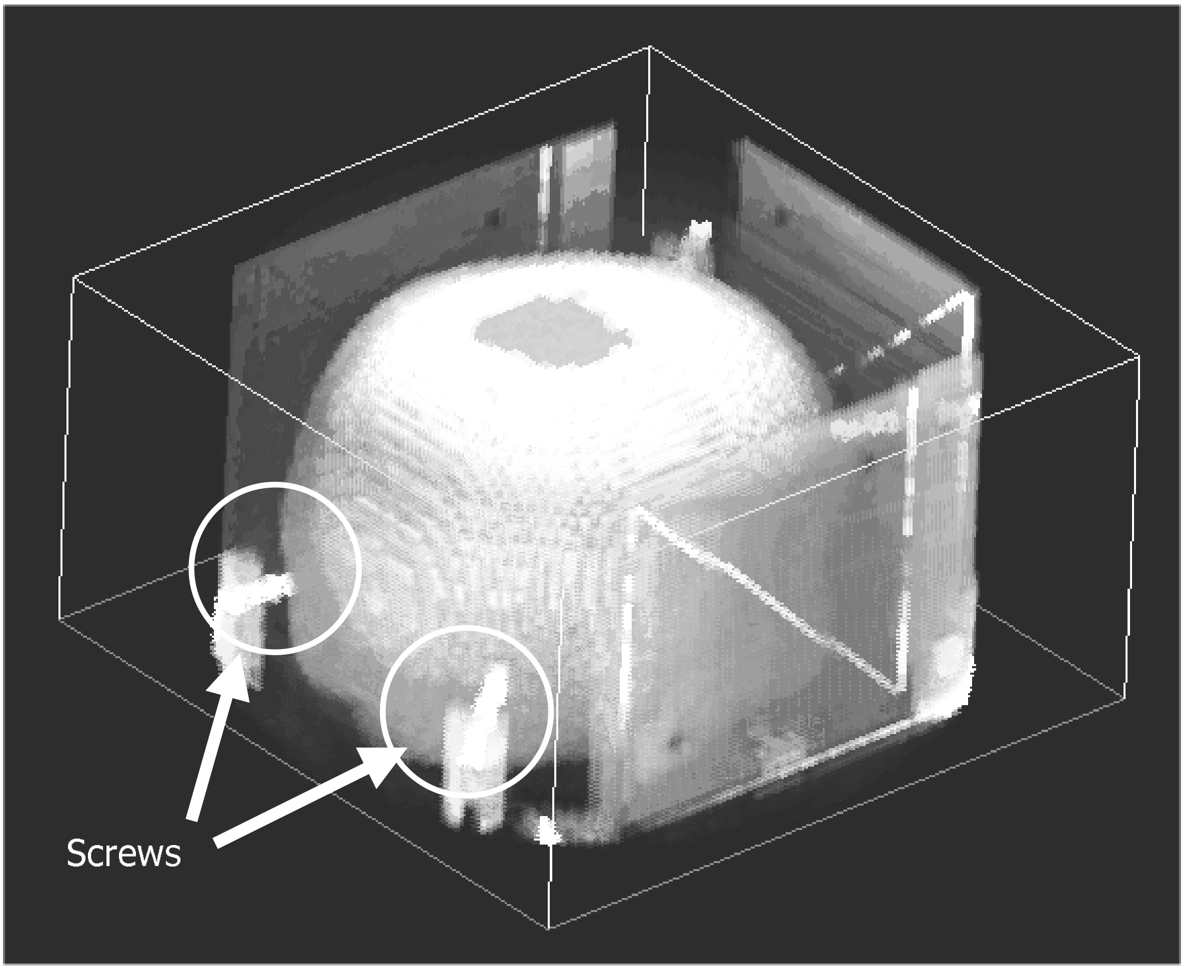

Figure 1. Volume rendering from a CT scan of a patient with the Leksell frame attached. The 'N' shaped markers allow to define X,Y and Z coordinates of any point within the patient's head. Attaching screws can also be recognized.

2. METHODOLOGY

The method for combining the two different imaging modalities involved in the study critical for the result. The target locations obtained from the MR must be translated into frame stereotactic coordinates by locating the references on the CT.

The registration process calculates the three-dimensional geometrical transformation that converts the coordinates of one image using the other as a reference. When both images are registered, the same coordinates correspond to the same anatomical location in the patient's head. There are several registration methods proposed for multimodality 3D images. Some of them rely on the location of anatomical landmarks by an expert [13] or on the use of fiducial markers visible on both modalities that are attached to the patient's skin [14]. Other methods calculate the geometric transformation automatically, using only the information contained in the image and avoiding any manual intervention or the use of marker devices [15-18].

In our case, a clinical MRI of the patient with no special requirements is used for the target location, avoiding the use of any external markers or reference frame during the acquisition. The day of the intervention a Leksell frame is attached to the patient's head and the a CT scan is performed with the aim of providing the reference for the coordinate calculation on the stereotactical system. The small slice thickness of the CT gives very precise location, and to avoid high radiation dose to the patient only the part of the head where the target will be found is acquired. Before the surgery, the images are registered using a recently developed automatic algorithm that is based on the maximization of the Mutual Information between the images[17, 18]. The registered images are then fused and the physicians locate the target on the MRI and obtain the stereotactical coordinates that come from the frame references in the CT image.

Once the CT acquisition is completed the images are sent through the hospital network to a PC workstation where the MRI was previously transmitted. The images are processed with software developed by our group. The neurosurgeons visualize them and proceed with the registration process.

3. IMAGE REGISTRATION

The algorithm used in this step is based on the maximization of Mutual Information (MI) initially proposed by [18] and [17]. Mutual Information is a concept taken from information theory that represents the degree of dependence of two random variables *A* and *B* by measuring the distance between the joint distribution $p_{AB}(a,b)$ and the distribution associated with the case of complete independence $p_A(a) \cdot p_B(b)$ [18]. This concept is related to the entropy of the random variables by the equation:

$$I(A,B) = H(A) + H(B) - H(A,B) = H(A) - H(A\,|\,B) = H(B) - H(B\,|\,A) \tag{1}$$

where *I(A,B)* represents the mutual information between *A* and *B*. *H(A)* and *H(B)* are the entropies of these random variables, *H(A,B)* their joint entropy, and *H(A|B)* and *H(B|A)* the conditional entropies. The entropy provides information on the amount of uncertainty about a random variable; *I(A,B)* is the reduction of uncertainty of a random variable *A* by the knowledge of another variable *B*. The entropies are calculated as:

$$H(A) = -\sum_{a} p_A(a) \cdot \log_2 p_A(a) \qquad H(A,B) = -\sum_{a,b} p_{AB}(a,b) \cdot \log_2 p_{AB}(a,b) \qquad (2)\ (3)$$

Working with images, the probability density function can be estimated by the histogram, usually very easy to obtain. The optimum geometrical transformation *T* that registers two images will maximize the information of one image that is explained by the other. If *B* is the image to be transformed and *A* is the reference, the aim of the algorithm is to find *T* that maximizes *I(A,T(B)*. Then the calculation of the registration corresponds to the maximization of MI depending on the parameters that describe the transformation. As in our study both images come from the same patient, the registration consists of a rigid body transformation (6 parameters: rotations around the three axis and three translations). For the calculation of the joint histogram we have followed [18], that estimates the joint histogram *H(A,T(B))* using partial volume interpolation. This interpolation scheme does not create new intensity values in every iteration of the optimization, improving the accuracy of the results as compared to nearest neighbor or trilinear interpolation.

Optimization is the next step: A multiresolution approach is used for faster and better results. The transformation parameters are calculated with progressive user selectable subsampling steps in the range 884, 442, 221, 111 (X, Y and Z subsampling). 442 and 221 steps were used in all the cases providing accurate results. The optimization strategy chosen was Simplex algorithm [19] that, according to [20], is a good compromise between speed and simplicity of implementation since it does not require evaluation of the MI gradient. The solution was found in 2.5 minutes on average on a standard PC workstation (Intel PIII 800 MHz., 256 Mb RAM).

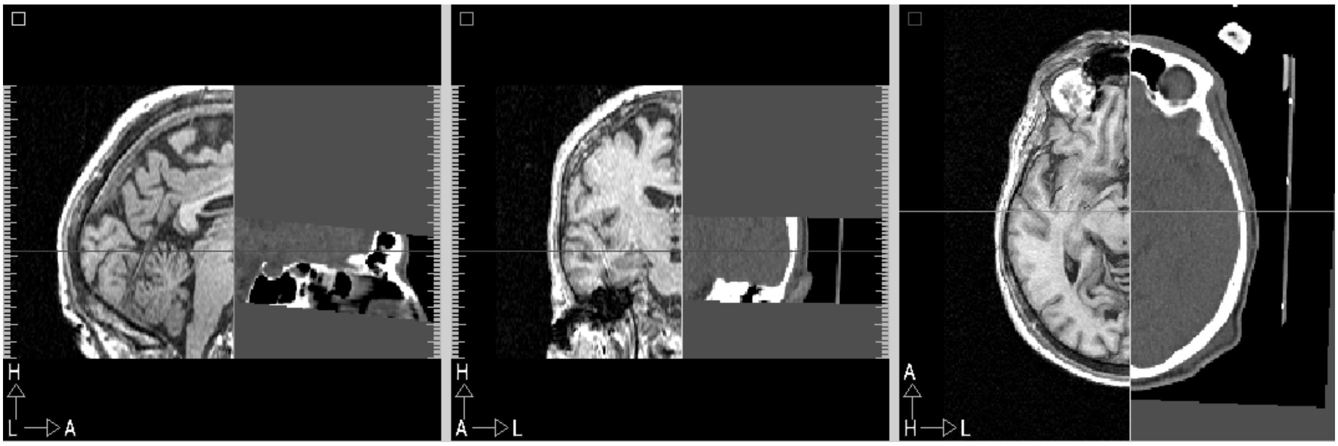

Figure 2. MR and CT images registered. Note the large difference in field of view that make necessary a pre-alignment step in order to find the right solution with the MI algorithm.

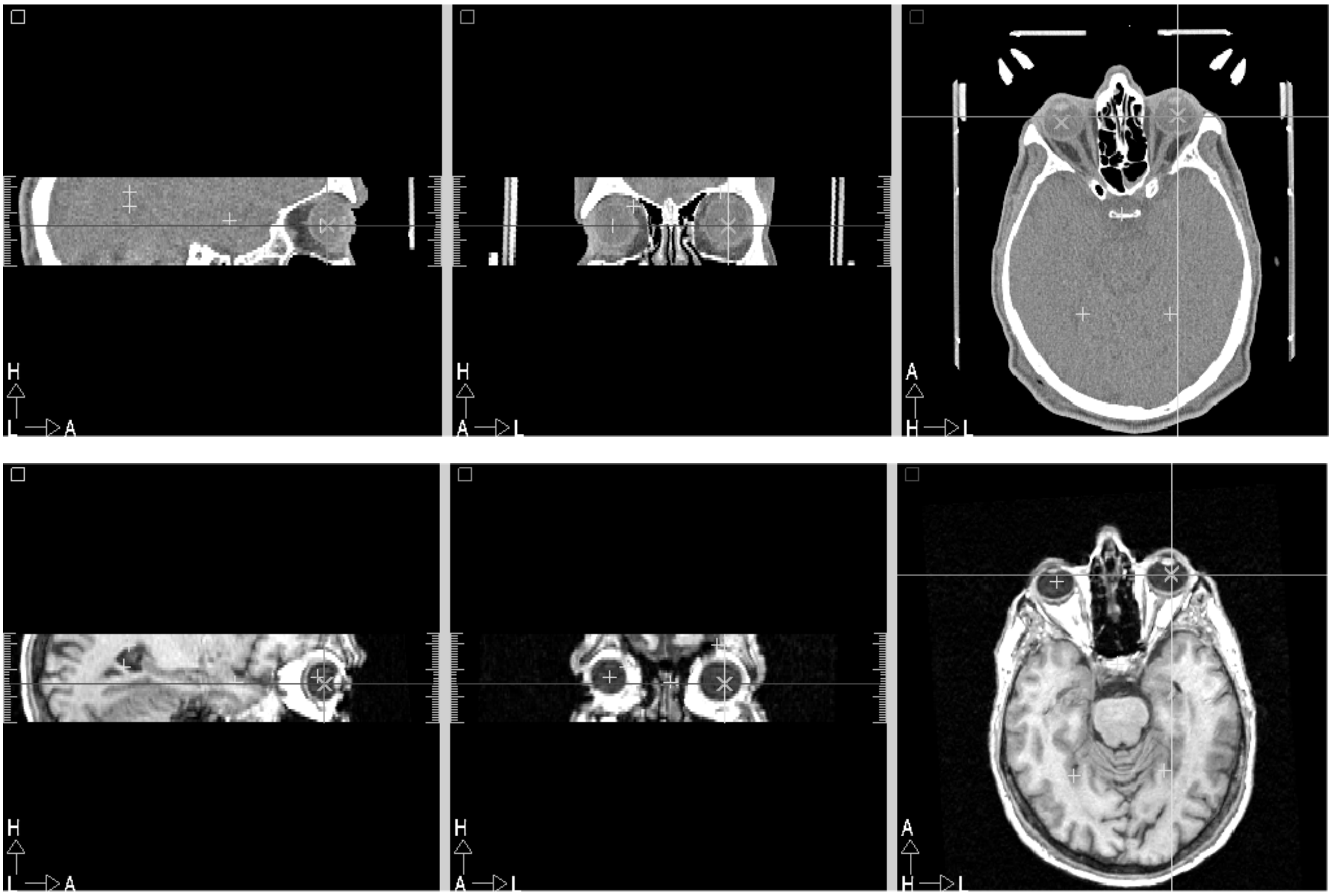

Figure 3. CT and MR images pre-aligned using 5 pairs of homologous points (SVD algorithm). This intermediate result is afterwards improved with the MI algorithm.

This registration method has the advantage of being modality independent, because no assumptions are made about the data values contained in the image. In our case, due to the difference in the field of view of the images to be registered (MR: complete brain; CT: only target area) (**Figure 2**), the automatic registration algorithm alone fails to find the right transformation. To overcome this problem, a pre-alignment step is performed. This process consists of a supervised reorientation of the volumes by selecting a minimum of three homologous pairs of points in both images. Because of the slice thickness of the CT scan, this image is usually very noisy. The pre-alignment does not need to be very precise, so it can be performed in less than two minutes and does not require special expertise. The transformation that relates the coordinates of these points is calculated using the SVD algorithm [21] (**Figure 3**). After this pre-register, the MI algorithm converged to the expected solution in all the studies. As a last step, the physicians display both images and check the quality of the registration process using a tri-planar viewer together with different visualization tools (**Figure 4** and **Figure 5**).

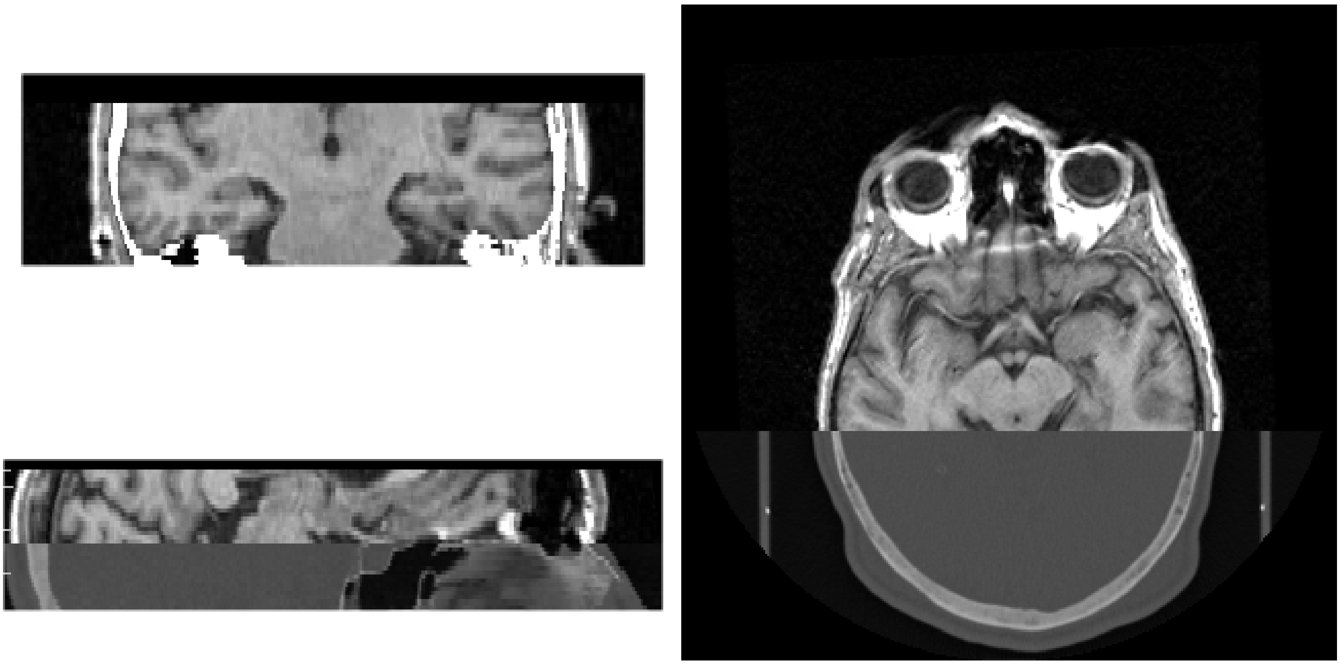

Figure 4. Different visualization tools are used to check the quality of the registration process: maximum value (*top left*); curtain mode (*bottom left*, *right*).

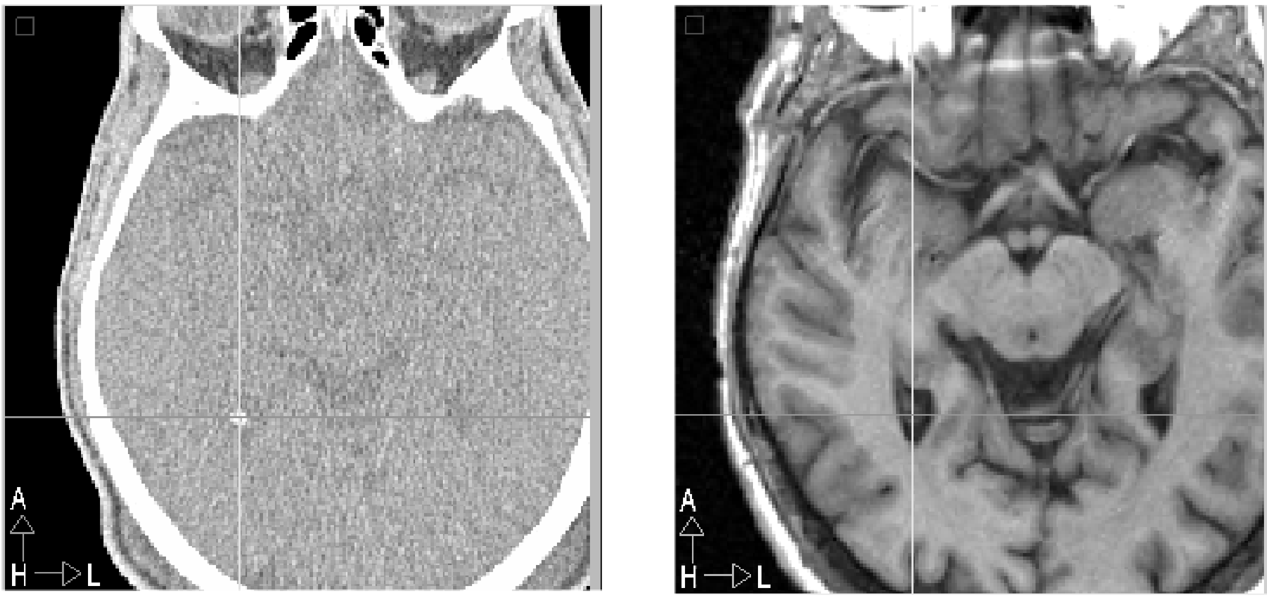

Figure 5. The position of known structures is displayed on the registered images in order to check the quality of the registration

4. TARGET LOCATION

Registered images are displayed together combining the MR anatomical information and the Leksell frame data coming from the CT scan. The design of the frame allows to find the stereotactic coordinates in any slice by locating the nine references as shown in **Figure 6**. Once the references are identified in the slice, and taking into account that the frame may be slightly rotated with respect to the image, the X,Y and Z stereotactic coordinates of any given point are calculated. With the notation depicted in **Figure 7**, the coordinates *P'x* and *P'y* of the point *P* are translated into the frame reference system (*Px* and *Py*) using the following equation:

$$\begin{pmatrix} P'x \\ P'y \end{pmatrix} = \begin{pmatrix} \cos\beta & -sen\theta \\ sen\beta & \cos\theta \end{pmatrix} \begin{pmatrix} Px \\ Py \end{pmatrix}$$

$$\begin{pmatrix} Px \\ Py \end{pmatrix} = \frac{1}{\cos(\theta-\beta)} \begin{pmatrix} \cos\theta & sen\theta \\ -sen\beta & \cos\beta \end{pmatrix} \begin{pmatrix} P'x \\ P'y \end{pmatrix}$$

Angles β and θ measure the rotation of the frame with respect to the image.

The Z coordinate is obtained from the distances 1-2, 8-9 and 4-5 (**Figure 6**), that can be translated into real measurements since the distances 1-3, 4-6 and 7-9 are all 120 mm (the size of the frame). These distances correspond to the Z coordinates of points 2, 5, and 8, contained in the image plane, that also contains the target *P*. In this way it is possible to obtain the Z coordinate of any possible target in the slice.

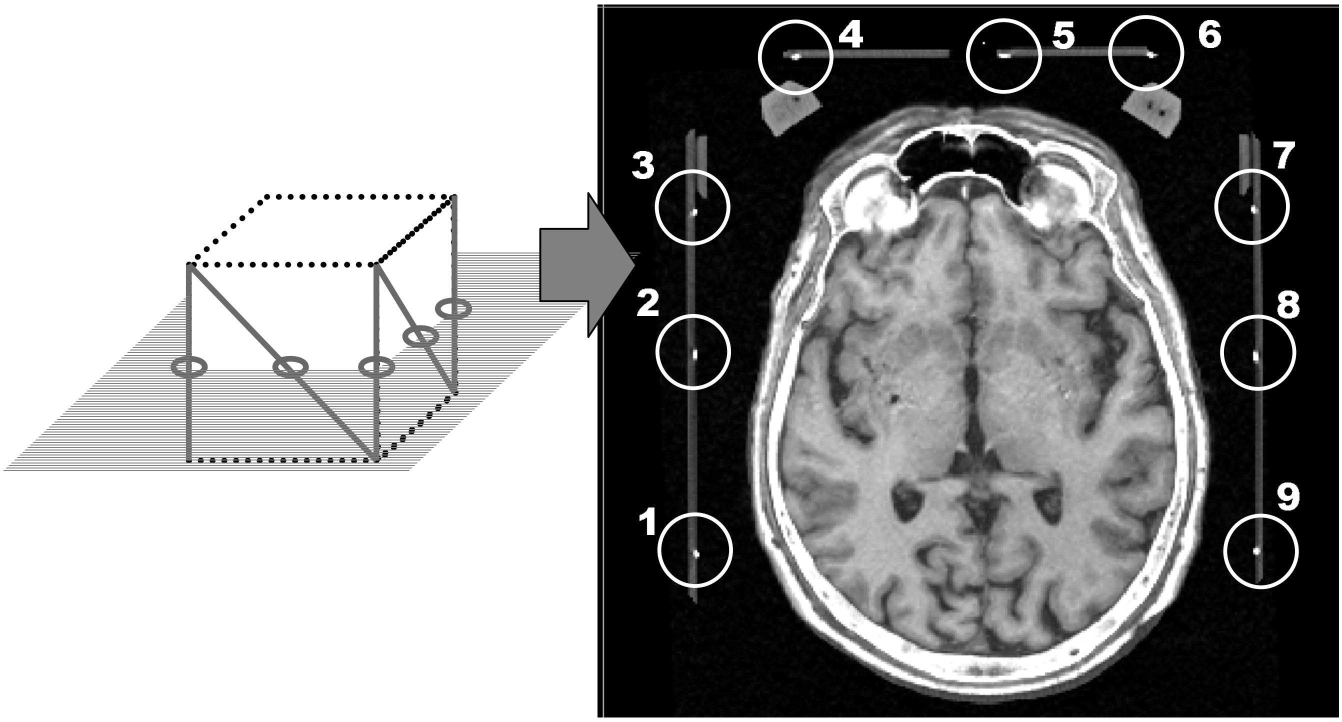

Figure 6 The Leksell frame has 'N' shaped markers in three planes. In every slice, the stereotactic coordinates are determined by the position of the 9 points.

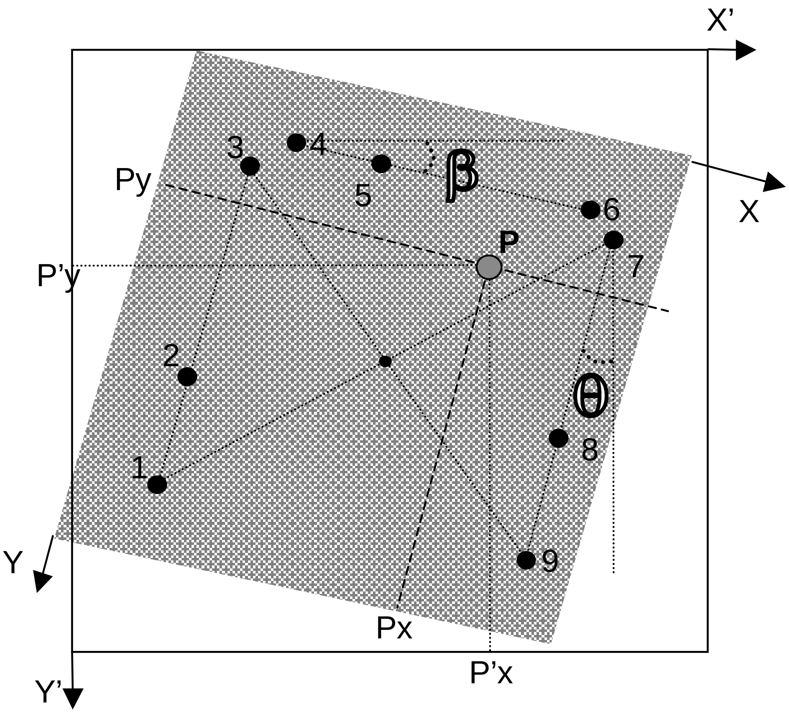

Figure 7. Target location in Leksell frame coordinates (X,Y) and image coordinates (X',Y'), with the nine references.

5. CLINICAL APPLICATION

The complete procedure has been applied to 10 patients suffering from movement disorders. A multidisciplinary group of neurologists, neurosurgeons, radiologists and engineers worked together in this project. In all the cases the surgical intervention was indicated as the best therapeutic procedure. For each study, an MR T1-weighted acquisition was obtained on a Philips GyroScan ACS 1.5 T. This study does not need any special requirements so it is usually part of the standard clinical imaging procedure on these patients. The day of the intervention, a Leksell frame was attached to the patient's head and a CT scan was acquired on a Philips LX Scanner. The slice thickness was 1.5 mm in all the studies and only the part of the brain where the lesion had been diagnosed was imaged. The average number of slices in the study was 30. This reduces the radiation dose compared to a whole brain scanning with the same slice thickness, while keeping very good spatial resolution.

In all the cases the automatic registration algorithm reached the expected solution after manual pre-alignment. The location of the targets was accurate enough, according to clinical criteria, although the surgical intervention after the target has been located is very complex and the protocol described is only one part of the process. The evaluation of the post-operative follow-up in these patients includes several factors, but in all cases there was a significant decrease of the movement disorders, and the physicians were satisfied with the results.

The complete protocol presented on this paper for image-guided neurosurgery has several advantages. The use of an MR image without stereotactic frame implies that the acquisition does not require any special consideration, and previous MRI studies of the patient may be valid for the purpose. By using the anatomical reference provided by MR, there is no need to image the whole brain with the CT, avoiding an excessive radiation dose. This is an important issue, as it allows to use a lower slice thickness, improving the accuracy in the location of the Leksell reference points at the expense of decreasing the SNR of the soft tissues (less important, since the anatomy is observed on the MR image).

The registration algorithm used has proved to be very accurate in multimodality imaging [20, 22], and the pre-processing step only increases the registration time in 2 minutes. Use of the SVD registration algorithm alone could have been an alternative, provided a large number of homologous points is selected in both images. However, this approach would have required a complete CT brain image, since it is very difficult to obtain sufficient precise anatomical references on the incomplete CT.

Further work includes the incorporation of a digital brain atlas to be registered with the patient images. This could help in selecting the proper target when it is difficult to identify it in the MR image.

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