Method for the evaluation of US perfusion for brain tumor surgery

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Abstract:

This paper presents a method to evaluate intraoperative ultrasound (iUS) perfusion imaging of brain tumors acquired during resection surgeries. It consists in comparing the iUS perfusion with the standard preoperative MR perfusion. In a first step the iUS and MR perfusion data are represented in a common frame with the same pixel size. This is performed using image registration methods to achieve a pixel-wise correspondence between both data sets. In a second step the perfusion data are analyzed and visualized with the SimVis framework. It is possible to select region of interests of the tumor, such as the margins or the center, and to perform a region-based comparison between the iUS and MR perfusion data. The pipeline is demonstrated for one representative surgical case.

Keywords: US perfusion, MR perfusion, brain tumor

1 Problem

Ultrasound (US) perfusion is an imaging modality used to analyze the perfusion of human tissue. This technique is in comparison to MR perfusion less heavy and can be easily used in the operating room. An ultrasound contrast agent constituted of gas micro-bubbles is injected and its absorption by the tissue is qualitatively (visually) or quantitatively analyzed in the temporal sequence of the US images. The quantitative analysis consists in plotting the image intensities measured at a given pixel over time and in computing different perfusion parameters from the obtained time-intensity curve. The most common parameters are the peak intensity, the time to peak, and the area under the curve corresponding to the cerebral blood volume. So far there is no standard for the choice of the most relevant parameters and their visualization [8].
An important medical application of perfusion imaging is its ability to differentiate lesions from healthy tissue. Ultrasound perfusion imaging is nowadays routinely performed for the detection and operation of hepatic lesions [10, 13]. Cerebral US perfusion is also beneficial for the transcranial examination of brain tumors [5, 6, 11, 12], and was moreover tested intraoperatively during tumor surgeries [4]. In comparison to B-mode ultrasound imaging, intraoperative US (iUS) perfusion enables to depict more accurately the tumor margins and is therefore a promising control tool for the detection of possible remnants of tumor tissue. This imaging modality needs however to be still evaluated in the context of brain tumor surgery. In this paper, we present a method for the evaluation of intraoperative US perfusion by comparison with a gold standard, namely preoperative MR perfusion.

2 Material and Methods

Perfusion data acquisition
One day before the brain tumor surgery, preoperative MR data of the patient are acquired. The examination includes 3D contrasted T1-weighted MR anatomical data (mostly isotropic) and 3D+t T2*-weighted MR perfusion data. The MR perfusion data consists of several volumes acquired at different points in time rendering the contrast agent accumulation visible. The in-plane resolution is 1.75 mm x 1.75 mm, the slice thickness is 5mm, and t is 40.
The tumor surgery is guided using a sononavigation system (Sononavigator, Localite, Sankt Augustin, Germany) and a conventional US device (AplioXG, Toshiba, Medical Systems Europe, Zoetermeer, Netherland). At the beginning of the intervention, the anatomical MR volume is registered with the patient based on anatomical landmarks and the result is improved using a head surface registration technique. At any moment the surgeon is able to acquire an iUS volume by scanning the region of interest using a tracked 2D US transducer. The acquired volume is superimposed on the preoperative MR data on the monitor of the sononavigation system.
During the surgery, right after the skull opening (craniotomy), a bolus of 1.5 ml of US contrast agent (SonoVue, Bracco s.p.a., Milano, Italy) is injected into the patient. Based on US B-mode images of the tumor, the surgeon localizes with the US transducer the cross-section plane situated at the tumor middle. The position of the probe in the patient coordinate system is identified through the navigation system. A temporal sequence of 2D iUS perfusion images is then acquired with at a rate of 19.0 frames per second over about one minute. The in-plane resolution is 0.35 mm x 0.35 mm.

iUS-perfusion and MR-perfusion data registration
Three main difficulties hamper the comparison of the iUS-perfusion data with the preoperative MR-perfusion data:

- The different data dimension: 2D+t data and 3D+t data;
- The differences in image size and in-plane resolution;
- The orientation of the data in different coordinate systems.

We propose a registration pipeline establishing a pixel-to-pixel correspondence between the iUS-perfusion data and a reformatted slice through the MR-perfusion data. All steps have been implemented in a prototypical application within the MeVisLab framework (MeVis Medical Solutions AG).

Step 1: preregistration. The cross-section plane corresponding to the 2D iUS perfusion data is registered with the preoperative anatomical 3D MR data using the transform matrix M_{sono} provided by the sononavigation system. However, the tumors in both data are offset due to the brain shift after craniotomy.
Step 2: brain shift correction. The tumor margin is manually delineated in the 2D iUS perfusion data (Figure 1, left) and in the anatomical 3D MR data resulting in two sets of contour points: P_{iUS} (2D) and P_{MR} (3D). An Iterative Closest Point (ICP) algorithm is used to register P_{iUS} to P_{MR} [1] using a rigid transformations and an isotropic scaling. It provides a transformation matrix $M_{shift,}$ which together with M_{sono} enables us to find the plane in the anatomical 3D MR data corresponding to the acquisition plane of the iUS perfusion data.
Step 3: plane correspondance. Then the anatomical 3D MR data are transformed into the MR perfusion frame. The MR data are acquired within the same protocol and are therefore represented in the same coordinate system but with differ-

ent in-plane resolution. A rigid registration is employed using a Newton-type optimizer and normalized mutual information to cope with the non-linear image intensity relations [2] and provides the transformation matrix M_{perf}. The matrix multiplication $M_{perf} \times M_{shift} \times M_{sono}$ yields the final transformation matrix M_{result}, which transforms the original iUS perfusion data into the corresponding plane in the MR perfusion data.
Step 4: pixel-wise correspondence. The MR perfusion data are resampled along the transformed iUS image plane leading to 2D+t MR perfusion data with the same x-y dimensions and the same in-plane resolution as the iUS data (Figure 1). A Trilinear interpolation is employed. A valid pixel-to-pixel correspondence in the iUS and MR perfusion images is obtained. Only the number of points in time still differs.

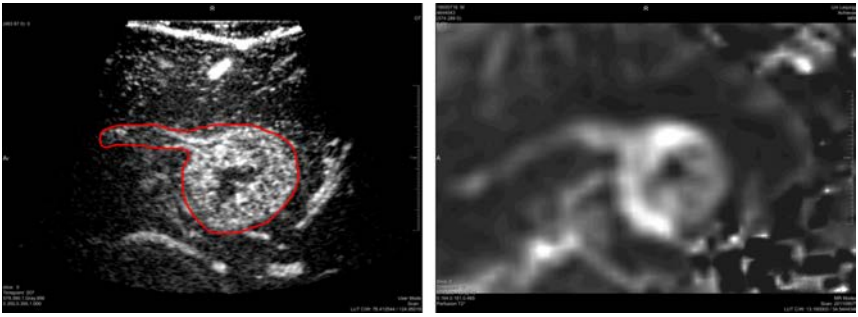

Figure 1: Registered intraoperative, contrast-enhanced Ultrasound (iUS) data (*left*) and preoperative MR perfusion data (*right*). The MR perfusion data has been resampled along the registered iUS image plane. The tumor margin is manually delineated in the iUS data and employed for registration as well as visualization purposes.

Intraoperative US-perfusion and MR-perfusion comparison
We compare iUS-perfusion and MR-perfusion based on perfusion parameters derived from the corresponding time-intensity curves [8]. Two pre-processing steps are carried out before parameter computation. First, the signal intensities of the T2*-weighted MR perfusion data are converted to contrast agent concentration [9]. This is a prerequisite for the determination of perfusion parameters, which are at least proportional to real quantitative hemodynamic parameters, such as cerebral blood volume and cerebral blood flow. Second, the iUS data is smoothed in the spatial as well as in the temporal domain to reduce the effects of strong speckle noise. A mean filter kernel of size 5 x 5 x 19, where 19 is the number of points in time, has been empirically determined as appropriate.
After the pre-processing, a set of seven perfusion parameters is computed pixel-wise from the iUS and the MR perfusion data [8]. The pre-processing and the parameter derivation have been implemented in MeVisLab. The fourteen 2D perfusion parameter images are aggregated for a concurrent interactive visual analysis and a comparison within the SimVis framework [3]. SimVis is a multiple coordinated view framework where each view is equipped with interactive drill-down operations for focusing on data features. Two classes of views are integrated: physical views, such as direct volume rendering, show information in the context of the spatiotemporal observation space while attribute views, such as scatter plots and histograms, show relationships between multiple data attributes. The user may drilldown the data by selecting interesting regions of the observation space or attribute ranges leading to a consistent highlighting of this selection in all other views (*brushing-and-linking*). SimVis has been applied to perfusion data in breast cancer diagnosis and in the diagnosis of ischemic stroke and Coronary Heart Disease [7].

3 Results

This pipeline was tested on data of a patient with a glioblastoma multiform located in the left frontal area of the brain. The iUS perfusion data reveals the enhanced tumor margins as well as a necrosis at the tumor center (Figure 1, left). For this patient T2*-weighted MR perfusion data are available.
A typical analysis session with SimVis is shown in Figure 2. The upper view shows the tumor in its spatial context. A gradient image of the point in time employed for tumor delineation in the iUS data serves as background (Figure 1, left). Blood vessels as well as the tumor itself appear elevated due to their high contrast agent accumulation at this point in time leading to a strong separation from the surrounding tissue, i.e. a high gradient. The whole tumor extent is indicated by a highly transparent layer in front of the gradient image. The current attribute selection is colored according to the area under the curve derived from the iUS data. The selection has been defined in the histogram view (lower middle). The histogram shows the results of an Euclidean distance transform, which determines for each pixel of the tumor

the distance to the surrounding tissue. High distances (dark bars) are brushed by means of a rectangular attribute selection thereby restricting the analysis to the center of the tumor. Moving the brush inside the histogram triggers an instant update of all other views and allows for a seamless inspection of tumor zones from the center to the margin.
The lower left scatter plot opposes the area under the curve of the iUS (x) and the MR (y) data. Each image pixel is represented by a colored dot. The transparency of each dot is modified with respect to the frequency of the underlying attribute pair. The current selection is rendered dark. Its shape illustrates the correlation of the chosen parameter between the two imaging modalities. The lower right parallel coordinates plot opposes three more pairs of perfusion parameters. The vertical axes are alternately associated with the parameter derived from the iUS and from the MR perfusion data, respectively. Each image pixel is represented by polyline connecting the axes. The current selection is rendered dark. The parallel coordinates facilitate a visualization of the entire high-dimensional space of perfusion parameters. From the course of the polylines, correlations as well as data clusters may be inferred. The current selection may be further refined by brushing the scatter plot and/or the parallel coordinates.

4 Discussion

The brain tumor tested here has an irregular shape, which is of benefit to the registration step. The appropriateness of the ICP algorithm for nearly spherical tumors, such as metastases, has to be investigated. Moreover, the success of the registration method is dependent on the manually performed tumor segmentations. It would be interesting to test the influence of slight changes to the tumor delineation. Further, it should be investigated whether perfusion parameters are best derived after resampling the MR perfusion data or before. In the latter case, they would be computed for each voxel

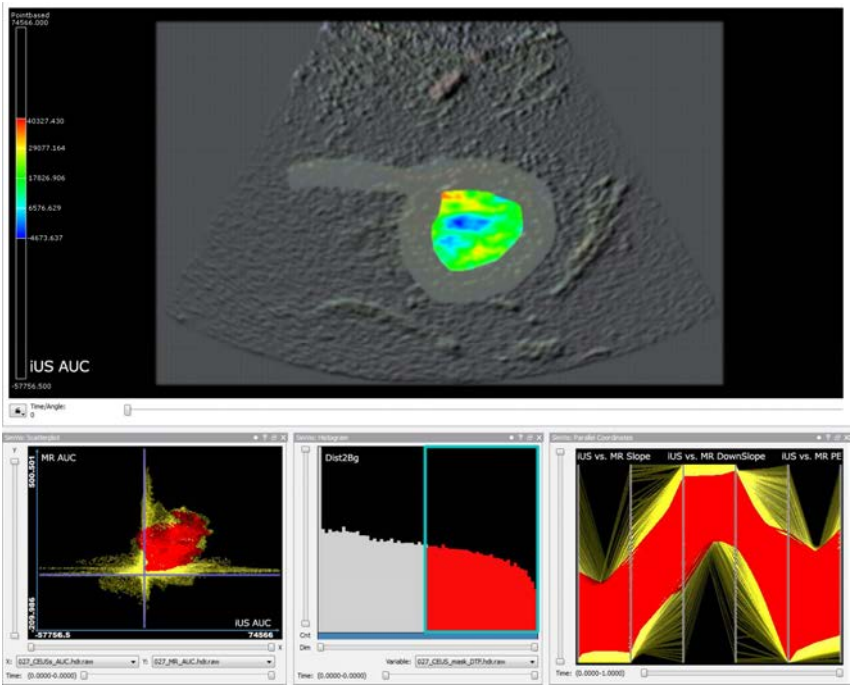

Figure 2: Concurrent, interactive visual analysis of perfusion parameters derived from intraoperative contrast-enhanced Ultrasound data (iUS) and preoperative MR perfusion data. The user may select and interesting range of parameter values within one or more of the attribute views (lower row) causing a colored emphasis of the associated tumor part in the spatial view (upper row).

and the resulting parameter volumes would then be resampled along the iUS image plane. So far, a mean filter was used to smooth the iUS perfusion data. Alternatively, fitting the perfusion curves with a gamma variate function could be more appropriate. This could attenuate as well the motion artifacts due to hand jittering during the intraoperative acquisition. Finally, the possible selection of further regions of interest in the image data such as blood vessels should be added.

5 Conclusion

In this paper, we presented a pipeline for the evaluation of intraoperative US perfusion data of patients with brain tumors. The pipeline consists of registration steps and an interactive visual analysis step. It facilitates a comparison of the perfusion parameters of the iUS perfusion data with those of the MR perfusion data based on a pixel-wise correspondence between the data. The implementation of the visual analysis step enables the user to select regions of interest of the tumor according to its anatomy, for example the margin or a possible necrosis, and according to its features, i.e. the perfusion parameters. Testing the pipeline on more patient data is required to improve the registration steps and the visualization and analysis of perfusion parameters according to clinical purposes.

6 References

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