Detection of areas with viable remnant tumor in postchemotherapy patients with Ewing's sarcoma by dynamic contrast-enhanced MRI using a neural network

M. Egmont-Petersen, J.P. Janssen, R. J. v. d. Geest, H.A. Vrooman, P.C.W. Hogendoorn, J.L. Bloem, J.H.C. Reiber
Leiden University Medical Center, Dept. of Radiology and Pathology, Div. of Image Processing, Leiden, the Netherlands
Email: michael@lkeb.azl.nl

Introduction

Dynamic contrast-enhanced MRI using an intravenous contrast tracer (Gd-DTPA) allows a detection of remnants of viable tumor (including small, scattered foci) in patients with high-grade Ewing's sarcoma. A high density of abnormal capillaries in viable tumor makes a distinction possible between viable tumor tissue and tumor parts that have been annihilated by chemotherapy.

In our hospital, the effects of chemotherapy on tumor size and perfusion is assessed from successive MR-examinations. The dynamic contrast-enhanced MR-sequence is analyzed by two-compartment pharmacokinetic modeling which results in estimates of the maximal signal enhancement, wash-in rate, wash-out rate and local arrival time of tracer in each voxel [1].

Pharmacokinetic analysis reduces the information in the underlying MR-signal $s(x,y,z,t)$ consisting of 51 dynamic samples to solely 3–4 pharmacokinetic parameters. However, all spatial information is left out of consideration because the parameters are estimated on a voxel-by-voxel basis. In this work, we investigate whether feed-forward neural networks can be trained to segment the (carefully preprocessed) dynamic MR-images into three types of tissue: healthy tissue, viable and nonviable tumor. Our gold standard is a histologic macroslice of which the orientation and position corresponds with the MR-section under study. The macroslice specifies the class label of each voxel.

Materials and Methods

After completion of preoperative chemotherapy, the MR-examination was performed on a 0.5 T super-conductive Gyroscan (Philips) using a surface coil. One, two or three sections were selected for T_1-weighted dynamic contrast-enhanced imaging using a magnetization prepared imaging gradient recalled echo technique. The MR-images were acquired with a repetition time (*TR*) of 12 msec, an echo time (*TE*) of 5.7 msec and a prepulse delay time of 741 msec. The flip angle was 30 degrees. The field of view varied per patient depending on the size of the tumor (200–450 mm), a 256×256 matrix was acquired. The slice thickness was 8 mm and the slice gap 12 mm. An intravenous injection bolus of the contrast tracer Gd-DTPA (Magnevist) was given followed by a saline flush. For each MR-section, 47 to 60 dynamic images were acquired with a temporal resolution of 3.3 sec.

Let $s(x,y,z,t)$, $t \in T$, denote the dynamic MR-signal obtained from voxel (x,y,z) at time t. The MR-signal is affected by both random and systematic distortions: the random noise induced by the MR-scan device, the postcontrast signal fluctuations caused by the heart beat, and other types of distortions intrinsic to the MR-technique. The postcontrast signal fluctuations are caused by a combination of a heterogeneous distribution of the bolus in the vascular compartment and the circulatory function of the vascular system. To reduce the random noise and, most important, to remove the systematic distortion component in $s(x,y,z,t)$, we use a nonlinear morphological filter [2]:

$$\bar{s}(x,y,z,w) = \frac{\max_{t' \in b}(\min_{t \in b}(s(x,y,z,t))) + \min_{t' \in b}(\max_{t \in b}(s(x,y,z,t)))}{2} \qquad (1)$$

with $b(t)=\{t-(w-1)/2,\ t+(w-1)/2\}$. The filter (1) has the property that high-frequent signal fluctuations (within the interval b) are removed but that large edges (caused by the wash-in and wash-out of tracer) remain unaffected.

Generally, the signal strength of $s(x,y,z,t)$ depends on several factors but the most important factor determining the signal amplitude and level (offset) is in our case the affine scaling performed by the (postprocessing) software on the MR-scanner. To reverse this scaling, the MR-signal is normalized as follows:

$$\hat{s}(x,y,z,t) = \bar{s}(x,y,z,t)\, r - l \qquad (2)$$

with r the rescale slope and l the offset, both present in the header files of the MR-images. The signal $\hat{s}(x,y,z,t)$ is uniformly resampled into a vector $\boldsymbol{a}(x,y,z)$ with 25 data points, each element $a_t(x,y,z)$ is provided as input to the neural network. The input vector to the neural network is concatenated with a vector $\boldsymbol{a}(x,y,z,\sigma^2)$ that is obtained from the dynamic MR-images after each image has been blurred with a Gaussian kernel (we chose the Gaussian kernel because it is the generating function in the linear scale space [3]). The blurred images add context-information to the neural network.

The correct class label of each voxel is obtained from the histologic macroslice. Registration is performed by computing the principal axes of manually delineated contours in the MR- and histologic images.

Results

The MR-images of five patients with Ewing's sarcoma, who underwent preoperative chemotherapy, were analyzed. The segmentation results (on a test set) obtained with the trained neural network are shown in table 1. It is clear that adding blurred versions of the MR-images to the neural network improves the segmentation result on the test voxels.

Table 1. Overall correctness and kappa computed on a test set consisting of 5 patients with Ewing's sarcoma.

Scale (mm)	0	5	8	10	12	15
Correctness	0.789	0.877	0.880	0.879	0.885	0.886
Kappa	0.516	0.565	0.581	0.567	0.583	0.596

An increasing scale of the Gauss kernel (width of σ^2 in mm) leads to an increasingly better segmentation. However, when too large a scale is used, small remnants (on a fine scale) tend to be overlooked. Therefore, we computed the estimated areas of viable tumor, the most important type of tissue one wants to identify, in each patient. The scale that resulted in the best area estimates (see table 2) is σ^2=10 mm. It is clear that the size of the remnants is related to the optimal size of the Gaussian kernel.

Table 2. Correct and estimated areas (measured in number of voxels) obtained by the neural network (σ^2=10 mm).

Patient	1	2	3	4	5
Area (Hist.)	180	227	0	31	326
Area (NN)	160	282	0	0	150
Rel. diff.	-11%	24%	0%	-100%	-54%

Conclusion

The results indicate that adding information from blurred MR-images to the neural network improves the segmentation. The analysis of the individual patients shows that the size of the Gaussian kernel determines the minimal size of remnants of viable tumor that can be detected. Our best results were obtained with a kernel size of σ^2=10 mm.

References

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