Evaluation of Surface-to-Core Perfusion in Cervical Cancer Tumors and the Role of Necrosis

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Tumor perfusion is commonly presumed to be poorest in the central portions (core) of the tumor, where hypoperfusion and necrosis may occur. Evaluation of the degree of tumor necrosis may reveal a relationship to the overall effectiveness of the chemo and/or radiation therapy (RT). In addition, tumors of different necrotic stages may suggest a line of therapy to be pursued such as RT that targets the active exterior tumor portion or necrotic tissue itself (1). The purpose of this current study is to measure the distance of each tumor pixel to the three dimensional surface of the tumor and correlate it with the signal intensity of the corresponding pixel on the perfusion imaging study, and (2) to apply the distance parameters to facilitate the localization and delineation of hypoperfusion/necrosis.

Materials & Methods: Our group has developed a semi-automated analysis techniques to evaluate both the location and extent of tumor necrosis in an effort to predict the effectiveness of different treatment modalities using gray-scale morphological operations Note figure on left of figure 1: Euclidean distances to the tumor perimeter were determined by minimum of ($d_i = \mathrm{sqrt}[a_1^2 (x-x_i)^2 + a_2^2 (y-y_i)^2 + a_3^2 (z-z_i)^2]$ which were calculated in 3D on a slice-by-slice basis and normalized to voxel dimensions; where a1, a2, and a3 represent the voxel spatial dimensions and each voxel point (xi, yi, zi) defines an edge value (figure 1). Morphological gray-scale distance operations were used to evaluate the complex 3D structures due to variations in both uterine and tumor anatomy (shown on left of figure 1). Plots were generated by using the corresponding distance measurement as the x-axis (binned) and the average contrast-enhancement response (as determined by averaging the signal intensity and smoothing over four distinct bins) as the y-axis (figure 2).

From a patient population of ten, approximately 30 magnetic resonance imaging studies representing pre-radiation therapy, 1-2 weeks post-radiation therapy, and 1-month post-radiation therapy were obtained. Each of these patients had an already-established diagnosis of cervical carcinoma. Tumors were delineated using a semi-automated detection method which provided a uniform delineation process while allowing for variability among the subjects' sensitivity to contrast enhancement. Specially-trained physicians with experience in gynecological imaging were assigned to delineate the tumors. Following delineation, the center of the tumor was automatically calculated using a centroid calculation. Our software enables this center to be replaced with a user-defined center when necessary.

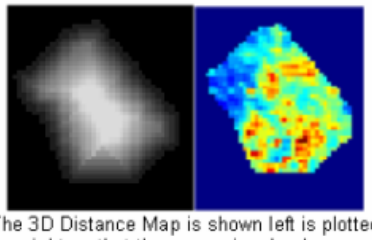

Figure 1: The 3D Distance Map is shown left is plotted against DCE values shown right so that the mean signal enhancement versus distance can be evaluated.

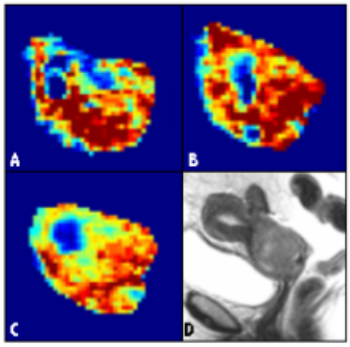

Figure 3: A, B, C: 3D Slices from DCE evaluation after enhancement determined. D illustrates zoomed in slice used for T2-weighted images used for tumor delineation.

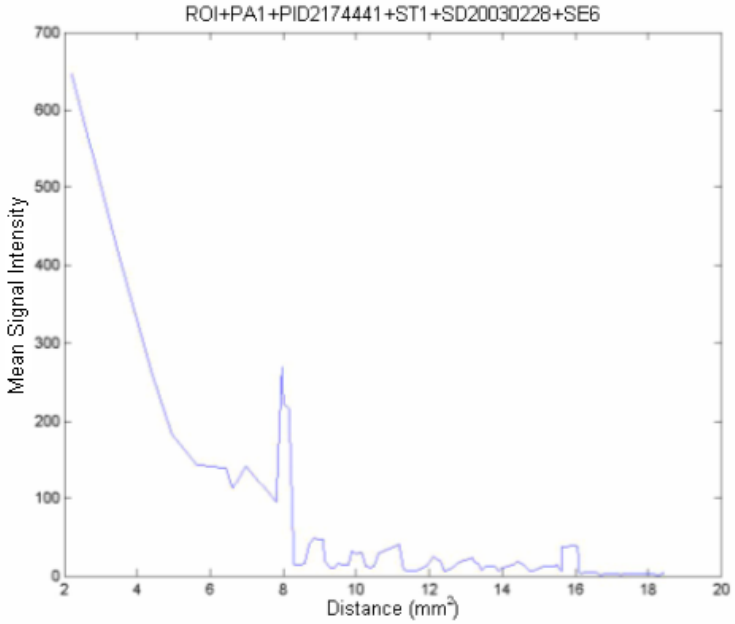

Figure 2: Illustrates the mean signal enhancement as a function of edge distance.

Results and Discussion: A rapid decline in the average signal intensity of perfusion is demonstrated in Figure 2 as imaging moves from the center of the tumor (farthest distance from the edge) to its surface (smaller distance values found along the left side of the graph). This result was found to be consistent across patients and across studies, thus offering both a qualitative and quantitative characterization of the nature and extent of tumor necrosis. Of key interest is the potential ability to characterize radiation necrosis and eventual response to therapy while the radiation therapy process is ongoing so as to allow appropriate therapeutic alterations. Figure 3 summarizes in 3D the effects on the tumor microcirculation. Overall, our preliminary work indicates that the evaluation of these tumors was a vital adjunct to treatment decisions. All therapy techniques rely on complex 'road maps' for accurate placement of RT or chemotherapeutic agents. By understanding the location and extent of necrosis, the overall activity of the tumor, therapies can be more accurately modulated in an effort to target active tumor and spare normal tissues.

References: 1. Warzocha K et al,. J Clin Oncol 1997;15(2):499-508.