Pharmacokinetic and R.S.I. Measures to Evaluate Regional Cervical Tumor Microcirculatory Response: Are There Systematic Differences in Contrast Uptake Patterns With Respect to Uterine Position?

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Purpose/Objective: Dynamic Contrast Enhanced-MRI (DCE) has been reported to be valuable in the evaluation of tumor perfusion in cervical cancer. However, while regional heterogeneity of tumor is well known (1)   such regional differences particularly related to anatomical location has not been reported when organ orientation is incorporated. The purpose of current study is to assess the heterogeneity of tumor and correlate the regional difference of tumor perfusion with the normal anatomic landmarks (2).

Materials/Methods: The DCE data from subdivisions of cervical cancer patients were evaluated prior and radiation therapy (n=18). Of those subjects who completed with the study to post-treatment (n=12) were considered. Each tumor was sectioned into eight three-dimensional subdivision wedges arrayed around the tumor center-of-volume. The orientation of the wedges was based upon uterine direction as determined by the projection of the endometrial canal and spatial orientation of the uterus. The tumor perfusion was estimated by the Relative Signal Intensity (RSI), which is defined by the ratio of the plateau post-injection signal intensity (SI) (at 75 seconds post-injection) divided by the pre-contrast SI on a pixel-by-pixel basis (3). Perfusion in each of eight subdivisions of the cervical cancers was estimated by the mean RSI within each region. Statistical differences among the various regional subdivisions were computed from RSI distributions within each region for cervical cancer patients pre-radiotherapy. The MR acquisition of the cervical cancer data has been previously well described (3). In this study, MR acquisition was performed on a Siemens 1.5T Vision (Erlangen, GDR) that included a T2 Turbo Spin Echo (T2-TSE) with the following parameters: TE=125 ms, TR=5 s FOV=25x40 at matrix 192x256. In accordance, dynamic contrast enhancement (DCE-MRI) images were acquired during bolus injection with 10 time frames of sagittal ST=8 mm, TE=5.0 ms, TR=12.0 ms, FA=30^0, FOV= 25x40 cm, matrix=138x256 and number of partitions=14 were matched to the T2-TSE images. The T2-TSE and DCE-MRI were matched spatially using standard 'sequence copy' available on the Siemens Vision[TM]. In the pre-radiation treatment patients, 18 were analyzed from a group of advanced cervical cancer patients using the parameters defined above. Out of 19 cases sampled, one case was excluded because the tumor was only delineable on two slices, which would not give a proper 3D representation for the tumor (final count of 18 pre-radiotherapy studies). Tumors and uterine positions were delineated by a physician on the T2-TSE images without direct visualization of the DCE data using our in-house analysis software written in Matlab (Natick, Ma) and Visual C++ (Microsoft, Redmond).

Results: Significant differences over the eight regional subdivisions among all tumors were found via a repeated-measures analysis of variance (ANOVA) design that produced an F-value=18.37 with DOF(7, 119) such that p<.0001 on the pre radiation treatment data. In addition, the difference along the cranial-ventral to   caudal-dorsal direction along a line approximating the uterine stripe was determined to be the greatest. A planned comparison contrast enhancement between the segments closest to the corpus of the uterus with those segments closer to the cervix demonstrates a significant difference t-value=3.19, p<0.002. No significant differences were found on the preplanned comparison data for horizontal segments (α=.05). On Pharmacokinetic amplitude and K_{pe} data there were detectable significant differences (F-value=6.92, p<.0001 and F<6.3, p<0.001). A post-contrast analysis of the K_{pe} data demonstrated that the K_{ep} had a t-value=-4.19; p<.0001 demonstrating that the segments proximal to cervix had more K_{ep} than the corpus segments. Additionally, the pharmacokinetic amplitude was determined to have a t-value=4.35; p<.0001. Perfusion estimates post-radiation did not did produce any notable changes on either RSI or pharmacokinetic measures.

Discussion: The overall test demonstrated significant statistical differences using the RSI value and K_{ep} across the eight different 3D sectors suggesting regional heterogeneity of tumor perfusion. Such differences are most pronounced between the segments closest to the corpus of the uterus (segments 8,3,4) and the three segments closest to the cervix (segments 5,6,7) of the tumor as compared left-right tumor direction evaluation. The etiology for such patterns of differences remains unknown. It may reflect the variation of angiogenesis and/or normal regional blood supply with richer blood supply to the body and corpus of the uterine and poorer blood supply to the cervix.
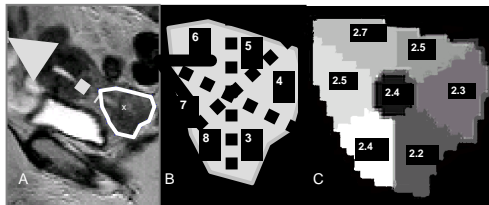

Figure 1: A) Shown in this image are the 6 segments within the primary-secondary plane. B) A more lateral slice cut which shows that includes the second segment (arrow) that covers the right segment. Note, that the first sector is not shown on either A or B because the first segment is on a opposite slice (left lateral to this slice). C) Demonstrates DCE over regions on a more lateral slice to illustrate 3D nature of the wedges.

Conclusions: The analysis of data suggest significant differences in tumor perfusion between macroscopic regional 3D wedge subdivisions within cervical tumors based on uterine position on pre-radiation treatment data. Regions nearest the corpus have significantly higher contrast uptake when compared with regions near the cervix. The pre-treatment data appeared to present the largest regional differences.   The study patients that died of the cervical cancer also mirrored the regional differences in cervical segments as compared to the corpus segments on the RSI signal and the K_{pe} signal on pre-radiation data. Post-radiation treatment data did not demonstrate significant differences as it is possibly affected by post-treatment inflammatory changes

References:
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