Metabolomic Imaging

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Introduction

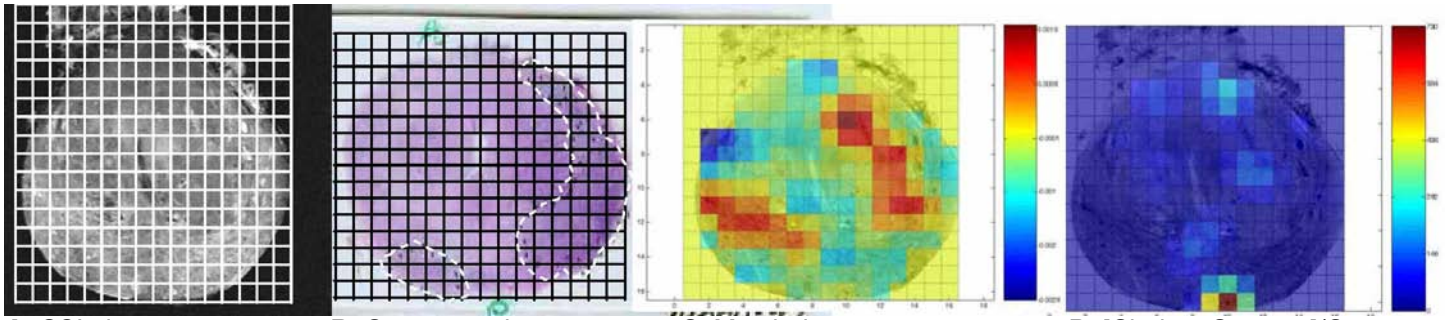
Current genomics evaluates thousands of genes simultaneously and correlates their genomic profiles, instead of the expression of a single gene, with a particular disease condition. In parallel, all the metabolite processes (pathways), or metabolomics, in a biological system, are also interconnected and should be evaluated simultaneously. The alterations of the overall metabolomic profiles are expected to be more sensitive and specific to a particular physiological and/or pathological condition than the change in any single metabolite. Metabolomic profile(s) defined by principal component analysis (PCA) of *ex vivo* MRS measurements of diseased specimens can aid *in vivo* disease detection; constructing these defined profiles with metabolite parameters measured by in vivo MRS (e.g. chemical shift imaging, CSI, or MRSI), and mapping the resulting values for all the voxels on a 2D or 3D anatomic image reflects degrees of disease involvements in the evaluated system.

Methods

Freshly removed human prostates from cancer patients were kept on ice and analyzed within two hours of surgery. Two- and three-dimensional CSI analyses were conducted at room temperature, on a 7.0 T scanner. After the analysis, specimens were fixed for histological evaluation. Metabolite intensities from CSI data for each voxel were processed by commercial softwares Nuts and Perch, and used to construct prostate cancer specific metabolomic profiles based on the published PCA results (*Cancer Res. 2005;**65**:3030-3034*). The values of the calculated PCs for each voxel were used as indices in the color-map to determine the color, and displayed transparently on an overlay of the anatomic image.

Results and Discussions

Six prostatectomy cases have been recruited in the study. Results from the first case and the potential powers of the metabolomic imaging are illustrated in the following figure. In this figure, (A) shows the placement of the CSI grid on the examined 2D cross-section of the prostate; (B) presents whole-mounted histopathology with tumor regions circled by white dotted lines; (C) displays the metabolomic image constructed with CSI data according to the published profiles (*Cancer Res. 2005;**65**:3030-3034*) with prostate cancer index in red; (D); presents a comparative image of the ratios of spectral regions choline-to-creatine vs. citrate, commonly used by MRSI (*Radiology 2004;**233:**701-708*), obtained from the same CSI data set.



A. CSI placement. **B.** Cancer in white regions. **C.** Metabolomic imaging. **D.** [Choline-Creatine]/Citrate.

The above presentation summarizes the general observations of the prostatectomy cases we have analyzed thus far. Metabolomic imaging indicates high intensities of cancer profiles in or around the regions where tumors are found by histopathology, which appear to be more accurate than the common choline-to-creatine vs. citrate ratio used by MRSI. This observation is clinically significant for there is still no single test that can detect the locations of cancer before histopathology, even in a removed prostate. However, when comparing individual voxels between (B) and (C), it is clear the correlation is not linear. This can be caused by many reasons, such as the facts that: in this pilot study we used cancer profiles obtained from tissue magic angle spinning spectra measured at higher field strength; there are susceptibility effects at the surface of the specimens and out-of-voxel effects; and the fixation of the specimens causes anatomic alteration that can affect co-registrations. We are working on addressing these issues.

Conclusion

We have demonstrated the potential of detecting cancer in removed human prostates by using the novel concept of metabolomic imaging. With additional systemic developments, we consider the *in vivo* application of the concept for clinical purposes, including disease diagnosis, to be imminent.

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