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MRI-BASED VIRTUAL HISTOPATHOLOGY FOR NON-INVASIVE DIAGNOSIS OF PROSTATE CANCER, GLIOBLASTOMA AND OTHER CONDITIONS

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Researchers in Prof. Sheng-Kwei (Victor) Song’s laboratory have developed diffusion histology imaging ("DHI"), a tool to provide a non-invasive diagnosis for accurately grading tumors and guiding treatment decisions. This “virtual histopathology” technology classifies microstructures in MRI images by combining DBSI (diffusion basis spectrum imaging) structural metrics with machine learning algorithms that accurately disentangle pathologies within an image voxel. These “diffusion fingerprints” can then be translated to detect various histological structures, mimicking the process of conventional histopathological analysis.

In prostate cancer, DHI is highly accurate in predicting the presence and aggressiveness of the disease, thus complementing and improving current tools for risk stratification and treatment planning. DHI can distinguish between normal, benign and tumor tissue; predict tumor location; and classify tumors with a Gleason grade score. This could overcome the major drawbacks of the standard of care diagnostics - false positives (from PSA screening) and uncomfortable, inaccurate needle biopsies that miss 20-30% of clinically significant tumors. In practice, DHI could enable timely and precise virtual biopsy following PSA screening; reduce false positives compared with current mpMRI; and eliminate repeat biopsies in patients with low-grade cancer who undergo active surveillance to monitor their tumor progression.

In glioblastoma, DHI can detect and characterize complex tumor histopathology to improve diagnostics; enhance surgical planning; monitor response to treatment; and assist clinicians in deciding on treatment options. Specifically, it can decipher the key histological features of the tumor microenvironment to measure tumor burden and differentiate pathological changes without an invasive biopsy.

Stage of Research

- **Prostate cancer** – Proof of concept studies in 101 patients with suspected prostate cancer demonstrated that DHI had great diagnostic sensitivity and specificity and could distinguish cancer from normal and benign tissue with high predictive accuracy in classifying Gleason grading group
- **Glioblastoma** – Proof of concept using histological validation demonstrated that DHI accurately predicted key features of the tumor microenvironment (high tumor cellularity, tumor necrosis and tumor infiltration with 87.5%, 89% and 93.4% accuracy respectively)
- **Other** – early work shows DHI is capable of classifying multiple sclerosis lesions

Applications

- **MRI for virtual histology** with end user applications such as:
    - **prostate cancer** diagnostics, staging, eliminating needle biopsy and active surveillance
    - **glioblastoma** diagnostics, guided biopsy, classification and prognostics for response to treatment

- **multiple sclerosis** classification of white matter lesions

Key Advantages

- **Non-invasive procedure –** eliminates risks and discomfort associated with biopsy
  - for prostate cancer, could prevent unnecessary surgery in patients with low grade tumor who are candidates for active surveillance
  - for glioblastoma, potential to aid in determining tumor recurrence vs. treatment response
- **Accurate, quantitative results** for improved clinical decision-making
  - sensitive and specific tissue differentiation with diffusion fingerprints
  - localizes tumor to improve efficiency of focal therapy
  - eliminates "blind spots" from needle biopsy
  - predicts Gleason grade in prostate cancer
  - mm-level resolution with no imaging agents

Publications:

- Ye Z, Price RL, Liu X, Lin J, Yang Q, Sun P, Wu AT, Wang L, Han RH, Song C, Yang R, Gary SE, Mao DD, Wallendorf M, Campian JL, Li JS, Dahiya S, Kim AH, Song SK. Diffusion Histology Imaging Combining Diffusion Basis Spectrum Imaging (DBSI) and Machine Learning Improves Detection and Classification of Glioblastoma Pathology. *Clin Cancer Res.* 2020 Jul 21. PubMed PMID: 32694155.
- Ye Z, George A, Wu AT, Niu X, Lin J, Adusumilli G, Naismith RT, Cross AH, Sun P, Song SK. Deep learning with diffusion basis spectrum imaging for classification of multiple sclerosis lesions. *Ann Clin Transl Neurol.* 2020 May;7(5):695-706. PubMed PMID: 32304291.

Patents: Quantitative differentiation of inflammation from solid tumors, heart and nerve injury (U.S. Patent Application, Publication No. US20180055408)

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