Hyperspectral stimulated Raman scattering microscopy for label-free brain imaging

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Abstract

Glioblastoma multiform (GBM) is the most common malignant primary brain tumor with a median overall survival of only ~14 months [1]. The poor prognosis is partly attributed to the existence of subtypes among GBMs, which shows significant differences in prognosis and response to treatment [2]. Currently, two subtypes of GBMs, proneural and mesenchymal have been identified based on gene or protein expression [3]. However, such a genetic profiling approach is usually slow, complex and prone to errors. In this work, we report the development of a hyperspectral stimulated Raman scattering (SRS) imaging technique for label-free imaging of mesenchymal and proneural subtypes of GBMs. The developed SRS imaging technique provides hyperspectral Raman image stacks (2800-3000cm^{-1}) within 20s by controlling the time delay between the chirped pump and Stokes beams. The resultant hyperspectral SRS image stacks are decomposed by multivariate curve resolution (MCR) analysis to identify distributions of lipids and proteins in proneural and mesenchymal GBMs, which uncovers their biomolecular differences. The principal components analysis (PCA) and linear discriminant analysis (LDA) together with the leave-one spectrum-out, cross-validation (LOSCV) is employed on hyperspectral SRS spectra, yielding a diagnostic sensitivity of 88.9% (28/36) and specificity of 96.7% (29/30) for differentiation between mesenchymal and proneural GBMs. This work shows great potential of the spectral-focusing hyperspectral stimulated Raman scattering (SRS) imaging technique for molecular subtyping of GBMs in a rapid manner.

References

[1] R. Stupp et al, "Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma," N. Engl. J. Med. 987–96 (2005).
[2] W. A. Freije, et al, "Gene expression profiling of gliomas strongly predicts survival," Cancer Res. 64, 6503–6510 (2004).
[3] H. S. Phillips, et al, "Molecular subclasses of high-grade glioma predict prognosis, delineate a pattern of disease progression, and resemble stages in neurogenesis," Cancer Cell 9, 157–173 (2006).