Fractal Structure in Volumetric Contrast Enhancement of Malignant Gliomas Correlates With Oxidative Metabolic Pathway Gene Expression

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Introduction

Fractal structure is found throughout many processes in nature, and often arises from sets of simple rules. We examined the contrast enhancement pattern in glioblastoma brain tumor MRIs for evidence of fractal structure, which might then be compared to expression of specific gene sets obtained from surgical specimens of each tumor.

Methods

Volumetric T1 post-contrast imaging was obtained in 39 patients prior to surgical resection of pathology-confirmed glioblastoma lesions. For each tumor, we calculated the fractal dimension (Minkowski–Bouligand dimension) using a box-counting (cubic scaling) approach. RNA expression microarray data from resected tissue were explored by gene set enrichment analysis (GSEA).

Results

We found robust evidence for fractal structure in the contrast enhancement pattern, with an average fractal dimension of 2.17±0.10, with a visually apparent split at 2.10. GSEA analysis showed a definitive association between this split in fractal dimension and 6 gene sets (of 4080), all 6 of which are linked to mitochondrial respiration/ATP production pathways.

Conclusions

There is fractal structure in the volumetric enhancement pattern of glioblastoma tumors, with dimension approximately 2.15. Variation in this fractal dimension, and therefore the complexity of contrast enhancement it reflects, is specifically associated with genetic correlates of a shift to glycolytic metabolism in tumor cells. Drugs that shift glioblastoma to oxidative metabolism have recently been identified as independent therapeutic agents as well as sensitizing agents for irradiation. Therefore, a radiogenomic marker of glucose metabolism, such as this fractal structure in enhancement, might help to guide individualized therapy.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) Describe the basic concept of fractal structure, and how it relates to contrast enhancement patterns in glioblastoma, 2) Describe how variation in fractal dimension correlates with expression in mitochondrial respiration/ATP production pathways, 3) Calculate fractal dimension in brain tumors at their own institution.

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