Support for Warburg's hypothesis using dynamic ^{18}F -FDG PET in oncology

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Dynamic PET/CT scanning of the liver was performed in two patients with liver metastases. On CT (a), contrast-enhancing lesions were seen. Early (0–2 min after injection) PET images (b) showed decreased FDG uptake by the metastases compared to the normal liver. Late (35–40 min after injection) PET images (c) showed no FDG uptake in the necrotic centre and increased uptake in perinecrotic tumour areas.

Based on the observation that cancer cells exhibit increased anaerobic glycolysis compared to normal cells, Warburg hypothesized that the cause of cancer is a defect in energy metabolism [1]. The delivery of oxygen/nutrients to tumours is compromised by the formation of leaky vessels, resulting in areas of hypoxia and poor perfusion. Yet cancer cells have the ability to adapt their metabolism to hypoxic conditions. This adaptation involves the hypoxia-inducible transcription factor (HIF) oxygen-sensing system. HIF-1 activation mediates hypoxia-induced increased glycolysis and overexpression of glucose transporters [2]. FDG PET imaging exploits the increased glucose uptake by tumours to monitor metabolism (late images). However, first-pass

FDG images provide an index of blood flow [3, 4]. Thus, discrepant FDG uptake by tumour cells between early and late PET images reflects the direct control of glucose transporter overexpression by hypoxia, resulting from poor perfusion (Warburg's hypothesis).

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