The role of iron oxide nanoparticles in the diagnosis of vascular diseases: A systematic review

Faith O. Alele, Theophilus I. Emeto

Background: Vascular diseases remain a cause of high patient mortality globally. Current diagnoses are often through contrast-enhanced computed tomography or magnetic resonance imaging (MRI) with approximately 80% sensitivity. Iron oxide nanoparticles are increasingly used in enhancing vascular disease diagnosis due to their ability to selectively deliver imaging agents to specific locations. This article describes studies investigating the use of iron oxide nanoparticles in the diagnosis of vascular diseases in humans. Method: A literature search was conducted to identify studies assessing the role of nanoparticles in the management of vascular diseases using PubMed from Jan 2011 to June 2016. The following search terms were applied “vascular diseases” AND “nanoparticles”. Human studies investigating the role of nanoparticles in vascular diseases were included. Studies excluded were ex vivo and in vitro human association studies, and non-English studies. Results: Nine out of 179 studies met the inclusion criteria. Sample size ranged from 1 to 23 median 14, inter-quartile range (IQR, 5.5 - 20.0). Five studies reported that ultra-small super paramagnetic iron oxide (USPIO) enhanced MRI assessment of vascularity, and macrophage content in atherosclerotic carotid plaques. Three studies demonstrated that ultra-small super paramagnetic iron oxide improved MRI diagnosis of myocardial infarction and allows the detection of the peri-infarct zone. One study did not support the latter findings. Conclusions: Iron oxide nanoparticles are effective at improving detection and diagnosis of vascular diseases, although the long term effects of these agents are not yet known.

Overexpression of Hif2α is sufficient to generate features of renal cell carcinoma

Nasir A. Shah1,2, Alex Sands3, Yoshiro Maezawa4, Joseph Ly5, Vera Eremina5, Susan E. Quaggin5

1The Townsville Hospital, Townsville, Queensland
2James Cook University, Townsville, Queensland
3Mackenzie Health, Richmond Hill, Canada
4Department of Clinical Cell Biology and Medicine, Chiba University Graduate School of Medicine, Chiba University Hospital, Chiba, Japan
5The Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital, Toronto, Ontario, Canada
6Feinberg Cardiovascular Research Institute and Division of Nephrology and Hypertension, Northwestern University, Chicago, USA

Background: Renal Cell Carcinoma (RCC) is the most common urogenital tumor, accounting for 3% of all adult malignancies, and is characterized by an increase in expression of hypoxia inducible factors (HIFs). In RCC, mutations in the VHL gene allow the HIFα subunits to escape degradation and translocate to the nucleus where they activate transcription of their target genes. Over 60 HIF target genes have been identified, which are involved in processes such as angiogenesis, erythropoiesis, glycolysis, apoptosis, and cell proliferation. Although both HIF1α and HIF2α are upregulated in RCC, it has been suggested that HIF2α plays a more critical role. Method: In this study we examined the contribution of HIF2α in renal tumorigenesis by generating a transgenic mouse model containing a mutated human HIF2α gene. Selective mutation of the Proline531 and Asparagine847 residues produced a stabilized HIF2α that escaped proteasomal degradation while remaining transcriptionally active. Under the control of the ROSA26, and Pax8 promoters, a reverse tetracycline-controlled system (rtTA) allowed for temporal control of whole body, and tubular-specific overexpression of HIF2α. Results: Increased expression of HIF2α in the renal tubular epithelium resulted in enhanced cellular proliferation, erythropoiesis, lipid-accumulation, and the rapid development of renal cysts that had lost markers of tubular epithelial differentiation – all features that are noted in the early stages of RCC. Conclusions: Taken together, these results suggest that HIF2α is a key player in the development of RCC, and a potential target for treatment of this disorder.