"Describe an innovation/research area in interventional radiology and discuss its impact on current/future IR practices"

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Since its inception, the field of interventional oncology (IO) has evolved rapidly. Procedures are supportive, such as image-guided biopsy[1] or disease-modifying like ablation[2]. Immuno-oncology is likewise an innovative cancer research field seeking to harness physiological anti-tumour immune responses. Synergy between the two disciplines offers huge treatment potential[3].

All IO therapies cause in-situ tumour necrosis and are varyingly immunogenic[4]. A unique tumour antigen fingerprint is released ultimately triggering an anti-tumour immune response. In effect, the tumour acts as its own in-vivo antigenic vaccine[5,6], contributing to the abscopal effect[7], whereby localised radiotherapy causes distant tumour regression[8].

This immune response is adaptive and primarily cell-mediated by CD8+ effector/'killer' T-cells, with clonal expansion of T-cells post-cryoablation seen in breast cancer[9]. In humans, radiofrequency ablation (RFA) of hepatocellular carcinomas (HCC) causes a rise in Type 1 'helper' CD4+ T-cells, involved in CD8+ co-stimulation[10]. Increases in natural killer (NK) cell numbers and functionality post-RFA was also shown to be a strong predictor of survival[11].

Antigen-scavenging from dead tumour cells following IO therapy requires additional contextual signals to generate a strong, systemic, anti-tumour immune response[12]. Combination immunotherapy can provide these necessary contextual signals and optimise the immune response to destroy residual neoplastic cells local or distant to the IO treatment site[13].

Much data on combined treatment with disease-modifying IO therapies and immunotherapy remains pre-clinical. However, human studies and pilot clinical trials show early promise. Research has focused on liver tumours, primarily HCC as its treatment often utilises IO therapies (e.g. RFA/transarterial chemoemobilisation; TACE)[14] and it responds to systemic immunotherapy (e.g. interferon-alpha)[15].

Preliminary human studies have combined RFA/TACE with various immunotherapies treating primary and secondary liver tumours. In advanced HCC, hepatic arterial infusion of immunostimulatory OK-432 at the time of embolization prolonged disease-free survival versus embolization alone[16]. Retrospective studies show a 25-month survival benefit in HCC patients who underwent either RFA or TACE with activated NK cells compared to RFA/TACE alone[17]. Phase 1 trials exploring the role of newer agents including immune checkpoint inhibitors (e.g. nivolumab) in combination with TACE for HCC are ongoing[18].

Similar results have been shown for metastatic liver disease, with a 4.3-month survival benefit seen in those treated with a combination of lipiodol and granulocyte macrophage-colony stimulating factor (GM-CSF) at the time of embolization compared to embolization alone[19].

Further research efforts must translate such promising findings into objective improvements in patient outcomes and broaden the focus from HCC to other tumours. The role of treatment sequencing also requires exploration to determine whether the synergist effects of immunotherapy are greatest as an adjuvant or neo-adjuvant immune primer to an IO procedure.

It is essential that we improve our understanding of the secondary biological responses to IO therapies which produce growth factors/cytokines involved in both immunogenic and pro-oncogenic pathways[20]. Understanding how tumour microenvironments influence immunogenic and tumourigenic responses to IO therapies allows us to minimise unwanted tumour-stimulating effects.

Incorporating immuno-oncology into interventional oncology practice holds vast potential for new, minimally-invasive, targeted and patient-specific cancer treatments; exciting innovations that the interventional radiologist can pioneer.

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