system consists of the MMPs and specific tissue inhibitors of metalloproteinases (TIMPs). Synthetic MMP inhibitors have been trialled with limited success. The study will determine the expression of MMP system components in colorectal tumour and pre-operative plasma samples and correlate these with tumour pathology and 15-year survival.
Methods: 100 paired tumour and normal tissue samples and 76 pre-operative plasma samples were analysed by ELISA for MMPs (-1, -2, -3, -7 and -9) and tissue inhibitors (TIMP-1, -2; ng/mg protein for tissue and ng/ml for plasma samples). Tissue and plasma levels were correlated with tumour pathology ($P<0.05$; Spearman's correlation coefficient) and 15-year survival analysis was performed (overall and disease-free; Kaplan Meier, $P<0.05$). The study had ethics committee approval.
Results: The levels of MMPs and TIMP-1 were all significantly greater in colorectal tumour tissue than the corresponding normal mucosa.
Tumour tissue levels of all MMPs correlated with Dukes stage and TIMP-1 with tumour depth. Preoperative plasma levels of TIMP-2 demonstrated a negative correlation with tumour differentiation.
Results of Kaplan Meier survival analysis found levels of active MMP-2 and MMP-9 in tumour tissue and MMP-7 in plasma samples significantly correlated with both overall and disease-free 15-year survival, with higher levels associated with poorer survival.
Conclusions: Tissue and pre-operative plasma levels of some MMP system components significantly correlated with the tumour histopathology, disease-free and overall 15-year survival.

35.
PHARMACOLOGICAL INHIBITION OF ACID CERAMIDASE; A NOVEL RADIOSENSITISER IN A 3D RECTAL CANCER MODEL

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Background: We have previously utilized proteomic and immuno-histochemical data to validate that high levels of acid ceramidase (AC) expression confers poorer neoadjuvant chemoradiotherapy response in rectal cancer. Biological (siRNA, plasmid) and pharmacological (Carmofur) AC manipulation validated altered responses of radiosensitivity in-vitro. LCL521, a novel small molecular inhibitor, specifically targets AC.
Methods: Optimal LCL521 dosing using standard ELISA activity assays with DMSO control was established in multiple colorectal cancer cell lines (HCT116, HT29, LIM1215). Western blotting confirmed altered expression of AC. Standard clonogenic assays assessed cell survival following increasing x-ray irradiation and change in spheroid volume to assess growth.
Results: ELISA revealed reduced expression of AC to 18% with 10μm LCL in HCT116, 12% HT29 and 30% LIM1215. 2-hour pre-treated clonogenic assays demonstrated reduced colony formation efficiency (colonies/number of cells plated−CFE) and improved radiosensitivity across cell lines. HT29 showed 0.758(CFE) control v 0.317(CFE) LCL at 1Gy, 0.441(CFE) control v 0.260(CFE) at 2Gy and 0.0250(CFE) control v 0.0119(CFE) LCL at 4Gy (p value=0.024). LCL521 dosing of spheroids improved radiosensitivity across cell lines (HCT116spheroid volume day 15 post-LCL521 $2.36x10^{-5}$mm v control $4.15x10^{-5}$mm).
Conclusions: Initial work demonstrates that pharmacological inhibition of AC with LCL521 produces comparative radiosensitizing effects in-vitro with these cell lines. This work further solidifies acid ceramidase as a potential therapeutic biomarker, however further work is needed to recapitulate these findings in more complex organoid models and ultimately in-vivo to establish a translatable clinical role in this setting.

36.
ACID CERAMIDASE AS A POTENTIAL BIOMARKER FOR LOCALLY ADVANCED RECTAL CANCER; IS APOPTOSIS THE MECHANISM?

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Background: We have previously utilized proteomic and immuno-histochemical data to validate that high levels of acid ceramidase (AC) expression confers poorer neoadjuvant chemoradiotherapy response in rectal cancer. Biological (siRNA knockdown, plasmid over-expression) and pharmacological (Carmofur, LCL521) AC manipulation validated altered responses of radiosensitivity in-vitro; further solidifying the potential of AC as a therapeutic biomarker through unknown mechanism.
Methods: siRNA AC knockdown was achieved in multiple colorectal cancer cell lines (HCT116, HT29, LIM1215), with non-targeting siRNA control, prior to irradiation. Cleaved PARP-1 fragments were detected and quantified using western blotting. Cell cycle analysis was performed using Attune NxT Flow Cytometry and propidium iodide staining (PI). Progressive apoptosis stage detection was achieved combining a PI and Annexin V stain.
Results: Western blotting confirmed increased PARP-1 cleavage fragments for siRNA AC across radiation doses compared to control (4.8-8.2fold increase ($p=<0.05$)). These findings were reproduced with treatment with AC inhibitor Carmofur. Cell cycle analysis demonstrated a pre-GO/1 spike compared to control; also potentially indicative of apoptosis. Annexin V staining showed a significant increase in cells of all stages of apoptosis at both 8 and 24hours post-irradiation.
Conclusions: Initial work suggests that AC expression may be linked to cell apoptosis post-irradiation. With much needed potential predictive or therapeutic biomarkers for rectal cancer, AC may be able to act as a target to improve response to neoadjuvant chemoradiotherapy and allow tailored treatment. Further work to fully understand the underlying mechanism is required to establish a clinical role.

75.
IS ONCOPLASTIC BREAST CONSERVING SURGERY ONCOLOGICALLY SAFE? A META-ANALYSIS OF 18,163 PATIENTS

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Background: The role of oncoplastic breast conserving surgery (OBCS) is that of a middle ground between standard breast conserving surgery (SBCS) and mastectomy - it allows adequate resection margins of tumours unsuitable for traditional breast conserving surgery whilst allowing for a better cosmetic outcome and a reduced morbidity rate when compared to a traditional mastectomy. However, due to this being a relatively new type of procedure, there is limited evidence on its oncological safety.
Methods: This study aims to compare oncological safety of OBCS with SBCS and mastectomy by examining the relative risk of cancer recurrence and re-operation rates. Literature search of Pubmed and Web of Science databases was conducted. Meta-Analysis was performed using R Statistical Software (www.r-project.org).
Results: 19 studies including 18,163 patients were included in the analysis. For the primary outcome measure of recurrence there was found to be no significant difference between the OBCS and SBCS or mastectomy (RR 0.861; 95% CI 0.640-1.160; $p<0.296$). The secondary outcome measure of re-operation was initially found to be significant in favour of OBCS (RR 0.64; 95% CI 0.46-0.89; $p<0.01$), however after adjustment for publication bias this was attenuated to an insignificant difference between the two study groups (RR 0.86; 95% CI 0.56-1.31; $p>0.05$).
Conclusions: For both recurrence of cancer and re-operation rate, there was not found to be a significant difference between OBCS and techniques that are more traditional. This would suggest that OBCS is of comparable oncological safety to more established operations and a useful option in suitable patients.

79.
ROLE OF BONE SCINTIGRAPHY IN ADDITION TO CT SCAN IN THE DETECTION OF BONE METASTASIS IN ADVANCED BREAST CANCER

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Background: The NICE guidelines (CG 81: 1.1.2& 1.1.3) updated in 2017; in spite of the above guidance, the current policy for detection of bone metastatic is not uniform in the entire country (UK), some centres count on staging CT of the chest, abdomen and pelvis (CT CAP) only but many still