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The role of perineural invasion in long-term survival in patients with pancreatic carcinoma. S Janes[1], A Zaitoun[2], J Prajafer[2], J Catton[3], D Lobo[3], B Rowlands[3]. [1]Department of General Surgery, Christchurch Hospital, Christchurch; [2]Department of Histopathology, Nottingham City Hospital, UK; [3]Division of Surgery, Nottingham City Hospital, UK.

Most pancreatic carcinomas demonstrate perineural invasion, however its prognostic significance is unclear. The aim of this study is to grade the severity of perineural invasion and correlate this with survival.

A prospective analysis of all resected pancreatic carcinomas (n = 44) in a UK teaching hospital was carried out from 1997–2001. Perineural invasion was graded 0 (absent) to 3 (severe). Factors predictive of hospital mortality and 5-year survival were determined (patient age, gender, pre-operative albumin/ bilirubin, operation blood loss/ duration, Townsend score, nodal status, vascular/ perineural invasion, tumour size and grade).

Hospital mortality (18%), was significantly higher for patients with albumin <35 g/L, operating time >5.25 hours, blood loss =5 litres, lowest quartile Townsend score and re-exploration. Multivariate analysis identified albumin <35 g/ dL, (odds ratio [OR] 22.5, p = 0.043), re-exploration (OR 30.3, p = 0.029) and lowest quartile Townsend score (OR 39.8, p = 0.018) as independent predictors of hospital mortality. Actuarial survival at 1, 3 and 5-years was 56%, 29% and 24%. Perineural invasion was present in 31 (70%) patients. Survival was significantly better for perineural invasion grade 0–1 than grade 2–3: median survival 37 versus 17 months respectively, p = 0.007. Five-year survival was significantly less with vascular invasion and tumours >2 cm. Cox proportional hazard analysis identified grade 2-3 perineural invasion as the only significant independent indicator of poor prognosis, hazard ratio 2.8 (95% CI 1.1–7.2) p = 0.031.

Grade 2-3 perineural invasion is a strong prognostic indicator of poor outcome in pancreatic cancer. Grading should become standard practice in reporting of pancreatic cancer.

Diencephalic amnesia and the contribution of different thalamic nuclei. A Mitchell[1,2,3], J Dalrymple-Alford[1,3]. [1]Christchurch Brain Research Group, Christchurch; [2]Foundation for Research, Science and Technology, New Zealand; [3]Department of Psychology, University of Canterbury, Christchurch.

Diencephalic amnesia occurs following thalamic injury, due to tumour, stroke or the alcoholic Korsakoff syndrome, but the neural basis of this disorder remains uncertain. Clinical and animal evidence has implicated either the mediodorsal, anterior, or intralaminar thalamic nuclei. We hypothesised that these medial thalamic nuclei should be grouped into three regions, which contribute to functionally segregated circuits implicated in different aspects of memory. To investigate this hypothesis

using a rat model, we performed highly localised, neurotoxic thalamic lesions followed by memory tests that are sensitive to hippocampal, amygdala or dorsal prefrontal cortex damage. Nine rats received lesions to the anterior region (anterior thalamic nuclei), part of a cortico-hippocampal-thalamic circuit. Ten rats had lesions to the lateral region (rostral intralaminar, central medial, and lateral mediodorsal nuclei), which contributes to a cortico-striatal-thalamic circuit. Ten rats received posterior region lesions (the remaining mediodorsal nuclei), to disrupt a cortico-amygdalo-thalamic circuit. Evidence for normal temporal order memory, which is sensitive to prefrontal cortex damage, was found in both the Anterior group and the 11 sham rats (p <0.001 and p <0.01, respectively), but not the Lateral and Posterior groups (p's >0.40).

The Anterior group was the only group impaired on a spatial memory task, consistent with hippocampal circuit dysfunction (p <0.0002), whereas only the Posterior group was impaired on a reward magnitude memory task, consistent with amygdala circuit dysfunction (p <0.002). These lesion-behaviour dissociations encourage a more comprehensive and inclusive approach to our understanding of diencephalic amnesia.

Effect of hypoxia on the vascular targeting agent, Combretastatin A-4-P. **G Dachs[1,2], A Steele[2], C Coralli[2], C Kanthou[2], Gillian M Tozer[2]. [1]Angiogenesis Research Group, Department of Pathology, Christchurch School of Medicine and Health Sciences, Christchurch; [2]Tumour Microcirculation Group, Gray Cancer Institute, Mount Vernon Hospital, Northwood, UK.**

Combretastatin A-4 phosphate (CA-4-P) is a tubulin-binding agent in clinical trials as a tumour vascular targeting agent. *In vitro* CA-4-P causes microtubule depolymerisation, actin stress fibres and cell cycle block due to interference with spindle formation during mitosis. In experimental tumours, CA-4-P causes a rapid and catastrophic shutdown of the established tumour vasculature leading to necrosis and secondary tumour cell death. However, a narrow viable rim of surviving tumour tissue remains, allowing a rapid regrowth of tumours.

Little is known of the effect of inherent tumour hypoxia on CA-4-P activity, and conversely, what effect CA-4-P-induced hypoxia has on tumour progression. We analysed protein accumulation of the main hypoxic transcription factor, hypoxia-inducible factor 1 (HIF-1) in two human carcinoma cell lines and two primary endothelial cell types following stimulation by severe hypoxia (anoxia). The cells were treated with CA-4-P at clinically relevant doses (0.001–1 μM). Trypan-blue exclusion assays were used to determine cell survival following anoxic CA-4-P treatment.

Western blot analysis of treated cell extracts showed a drug dose dependent reduction in HIF-1 accumulation in hypoxic cells. This effect, although somewhat variable, was evident both when the cells were hypoxia-stimulated at the start or end of the CA-4-P treatment period. Cycling cells showed a reduced number of viable cells following CA-4-P treatment, whereas non-cycling cells, either due to cell density or long term anoxic incubation, did not respond.

In conclusion, it appears that CA-4-P treatment modulates HIF-1 accumulation. The subsequent effect on down-stream gene expression is currently under investigation.

An innovative system for rapidly reporting the FM 100-hue colour vision test. R Hidayat[1], R Hidajat[2], J McLay[2], D Goode[3], M Elder[2]. [1]Applied Computing Department, Lincoln University, Lincoln; [2]Department of Ophthalmology, Christchurch Hospital, Christchurch; [3]Department of Medical Physics and Bioengineering, Christchurch Hospital, Christchurch.

The Farnsworth-Munsell (FM) 100-hue test is globally accepted as one of the most sensitive and specific methods for assessing colour vision. It can detect ophthalmic disease (glaucoma, diabetic retinopathy, optic nerve lesions) at an early stage and has the added advantage of being non-invasive. However a major shortcoming of the test is the laborious and time consuming effort needed to calculate the results and to plot them on a chart for interpretation.

We have developed a computer program for reporting the FM test which also allows the patient's data to be read with a bar code scanner. This new system has been in routine use in eye clinics at Christchurch Hospital for one year and has proved to be of great assistance both in saving time and eliminating arithmetic errors in the scoring calculations. It produces the two reports, one for each eye, in four minutes which contrasts with the 60 minutes required by the conventional manual reporting system. Such a substantial saving in time will encourage clinicians to make greater use of this valuable diagnostic test.

Significantly our computer generated report duplicates the conventional manual report, the report clinicians are familiar with, and in addition indicates whether the results fall within the normal range appropriate for the patient's age.