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Letters

Effect of Temperature on Liver Tumour Blood Flow

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To EXAMINE liver tumour blood flow [1–3], the use of blood-flow microspheres and other methodologies requires the cannulation of peripheral vessels for the introduction of tracers and removal of a reference blood sample. Thus the ratio of blood flow in the growing edge of tumour compared with the normal liver tissue (T/N) can be measured but the results are widely variable. These studies often require extensive exposure of the liver and its resident tumours to ambient conditions while gaining entry into the arterial supply. This exposure may continue during blood-flow measurement and result in temperature fluctuations in the liver. We have studied whether these temperature changes influence the distribution of blood flow within the liver and tumour.

10 New Zealand white rabbits had VX2 carcinoma implanted into the right and left medial lobes of the liver. Radioactive blood-flow tracer microspheres ("Nentrac", New England Nuclear) were used to measure blood flow in both tumour tissue and in the surrounding normal liver (18 days postimplantation) in 5 rabbits with the abdomen kept closed and in 5 animals after laparotomy. The closed-abdomen group had tracer microspheres injected into the left side of the heart and 5 min later were killed. The open-abdomen group had a midline incision extending from below the umbilicus to the sternum, which was kept retracted to maintain exposure of the liver and *in situ* tumours to emulate some clinical and experimental conditions. Fluoroptic temperature probes (Luxtron, California) were inserted via the femoral vein and, in the open-abdomen group, also into the tumour and the normal liver tissue. Immediately after placement of the temperature probes the open-abdomen group were injected with tracer microspheres and 5 min later were killed. The liver was removed and divided into 1–2 g samples of either tumour tissue or normal tissue of the same lobe.

The mean blood flow in the tumour tissue of the closed-abdomen animals was significantly higher ($P < 0.0005$, two-tailed t test) than that in the tumour tissue of the animals with exposed livers (Table 1). The difference was about seven-fold but there was no variation in the associated normal tissue blood flows. These normal tissue blood flows were lower than the tumour blood flow in the closed-abdomen animals but had a greater mean flow than that in the tumour in the open-abdomen group. The closed-abdomen rabbits therefore had a significantly greater T/N ratio than their counterparts that underwent laparotomy ($P < 0.0005$, t test).

Table 1. Changes in hepatic arterial blood flow in tumour and normal tissue

	Closed abdomen		Open abdomen	
	Blood flow*	Temp (°C)	Blood flow	Temp (°C)
Tumour tissue	178.9 (70.2)	38.2 (0.4)	23.5 (9.7)	31.2 (4.2)
Normal tissue	31.2 (29.6)	38.2 (0.4)	31.4 (16.1)	34.1 (1.5)
T/N ratio	20.7 (21.6)	—	0.9 (0.6)	—

Mean (S.D.).
*Blood flow in ml per 100 g per min.

The changes in mean blood flow were reflected in the variations measured in tissue temperatures. At normal body temperature in the closed-abdomen animals the T/N ratio was high. In the short time (about 4 min) that the liver was fully exposed to room temperature (22°C) the tissue temperatures dropped. The core temperature of these animals was only slightly diminished (37.7 [S.D. 1.0]°C) but the tumour temperature and the normal tissue temperature were both significantly reduced ($P = 0.005$, t test). In addition, the tumour temperature of this group was significantly ($P = 0.02$, t test) lower than the normal tissue temperature.

The open-abdomen group can be regarded as a control situation when some form of tumour treatment is to follow. The tumour blood-flow decrease after laparotomy was highly significant. The T/N ratio is important in determining the proportion of any blood-transported anti-cancer agents preferentially reaching the tumour. We found a drop in mean T/N ratio in the rabbit tumours from approximately 20:1 to 1:1. This decrease would effectively eliminate any therapeutic advantage achieved by hepatic tumours being mostly supplied arterially compared with normal tissue, which is predominantly supplied by the portal vein.

It is difficult to establish whether the measured changes in tumour or normal tissue temperature caused the reduction in tumour blood flow or whether they simply reflect the reduced blood flow causing the drop in temperature. The blood flow in the normal tissue was unchanged after laparotomy, despite a significant decrease in temperature. Since the tumour temperature was significantly lower again compared with normal liver, there may be a threshold below which blood flow is influenced (i.e. under 34°C). The lack of haemodynamic autoregulation in tumour vasculature may also be relevant [3].

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1. Burton MA, Gray BN. Redistribution of blood flow in experimental hepatic tumours with noradrenaline and propranolol. *Br J Cancer* 1987, **56**, 585–588.
2. Burton MA, Gray BN, Klemp PF, *et al.* Selective internal radiation therapy: Distribution of radiation in the liver. *Eur J Cancer Clin Oncol* 1989, **25**, 1487–1491.
3. Krylova NV. Microcirculatory mechanisms in experimental tumours. *Bibl Anat* 1977, **15**, 285–287.

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