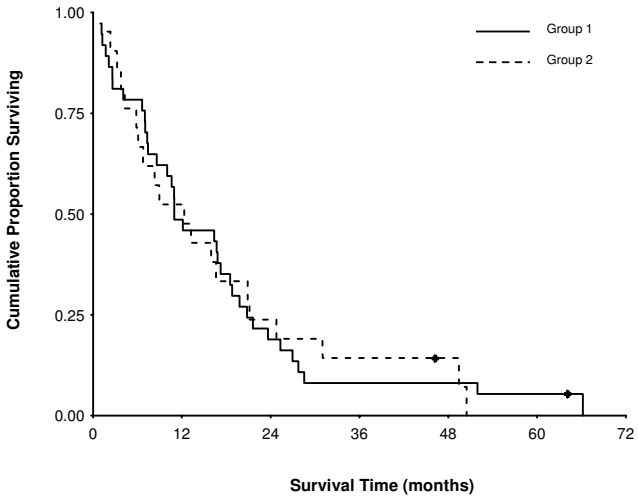

Figure 5
Kaplan-Meier survival curves for Group 1 patients ("hot" lesions) and Group 2 patients ("equivocal" or "cold" lesions). There is no statistical difference in cumulative survival by logrank test.

mal liver and therefore appear "hot" on an MAA perfusion scan. Patient characteristics and tumour stage, grade and extent do not appear to influence tumour vascularity as judged by TNR.

Early studies of internal radiation therapy reported that patients with relatively avascular tumours, as demonstrated by arteriography, did not respond as well as those patients with moderately to highly vascular tumours [18,19]. These studies, however, involved relatively small numbers and included patients with a variety of different primary cancers. Furthermore arteriography may not be a particularly accurate way of assessing tumour blood flow. The relationship between vascularity of CRC hepatic tumours and response to HAC has been studied by a number of groups. An early study by Kim et al observed that the more vascular the hepatic tumour on angiogram, the better the prognosis following hepatic artery ligation and infusional chemotherapy [20]. Subsequently, a number of authors [8-10] described a correlation between perfusion of CRC liver metastases, measured by ^{99m}Tc-MAA scans, and response to HAC. They concluded that increased tumour perfusion allows for a higher response rate from this particular treatment modality. Lehner et al on the other hand, found no correlation between tumour vascularity, as indicated by ^{99m}Tc-MAA scan, and response or survival following HAC in a study involving 36 patients with CRC liver metastases. They suggested that the degree of neo-vascularisation may only be demonstrated by super-selective catheterisation and questioned whether perfusion studies by angiogram or ^{99m}Tc-MAA reliably reproduce the perfusion pattern produced by the much slower flow rate used for chemotherapy [11]. In a relatively recent publication Dancey et al reported a better response of non-resectable HCC to SIRT with Theraspheres® for patients with "hot" lesions on MAA scan, than those with "cold" lesions [15].

The present study relates to SIRT in CRC metastases and has adopted a more methodical approach to assessing the question than that taken in Dancey's report of SIRT in HCC, and includes a larger number of patients. Not only have we attempted to quantify the MAA uptake more precisely, but we have also attempted to quantify the tumour response more precisely using changes in tumour marker after SIRT. The findings are clear. With the doses used there is no correlation between MAA uptake into CRC liver metastases prior to SIRT (TNR) and response to the treatment in terms of tumour marker data, CT data or survival time. Intuitively, one might have expected the opposite finding. The most obvious implication of this is that the doses of SIR-spheres® being administered may be higher than is required for obtaining a response in most patients. This possibility should be investigated. Comparison between the findings of our and Dancey's study suggests a higher dose of ^{90}Y microspheres is required for therapeutic effect in HCC than CRC. The fact that the SIR-spheres® were administered to the patients after giving angiotensin 2 into the hepatic artery, whereas the MAA perfusion scans were performed without angiotensin 2, potentially confounds the results and is unfortunately a weakness arising out of the retrospective nature of the study. The vasoconstriction achieved by angiotensin 2 has been shown to assist selective tumour uptake [21] and provides the theoretical basis for its use. Most units delivering SIRT do not use angiotensin 2 as it is no longer readily available and this does not obviously compromise results. The authors feel it is unlikely that the lack of correlation between TNR uptake of MAA and tumour response to SIRT would be accounted for by the administration of angiotensin 2, but it remains a possibility. If a positive correlation between the pattern of MAA uptake and tumour response was subsequently shown by another group, not using angiotensin 2, an argument might be raised supporting the routine use of a vasoconstrictor during SIRT. We currently use a bolus dose of phenylephrine hydrochloride 100 μg in lieu of angiotensin 2, on the grounds this may be of value, and no harm is conferred.

We have observed and previously reported that patients receiving SIRT using the dosing schedule of the present study suffer profound lethargy and anorexia for up to 4–6 weeks after the treatment [2]. The present study provides data to indicate that damage is sustained by normal hepatocytes, as indicated by a significant transaminase rise, after SIRT. There is however, no indication that the extent