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Re: Quantitative Hepatic Arterial Perfusion Scintigraphy and Starch Microspheres in Cancer Therapy

In their recent paper (*1*), Ziessman et al. described an innovative addition to intraarterial chemotherapy of hepatic tumors. They proposed infusing degradable starch microspheres (DSM) into the hepatic artery, together with the chemotherapeutic agent, so as to slow hepatic arterial flow and increase contact time between drug and tumor. They pointed out that this effect would be achieved only if there was no offsetting increase in shunting away from the liver, and they desribed infusion of Tc-99m macroaggregated albumin (Tc-99m MAA) with DSM, to detect any changes in shunting.

Chemotherapeutic tumor dose is determined by the fraction of injected drug that reaches the tumor and by the duration of tumor exposure to the drug. Vascular occlusion by DSM attempts to increase tumor dose by prolonging exposure, while increase in extrahepatic shunting would decrease tumor dose by decreasing the fraction of drug reaching the target. It is necessary to measure extrahepatic shunting, and one must also measure intrahepatic flow distribution, as this is equally important in determining tumor dose. Intraarterial infusion of Tc-99m MAA shows that there is preferential perfusion of tumor in many patients (Fig. 1). Kaplan et al. (*2*) have shown that this pattern of preferential perfusion is associated with a positive response to hepatic-artery chemotherapy, whereas poor or absent perfusion is associated with no response. It is important that intraarterial injection of DSM not redistribute flow away from tumor towards normal liver, as this would

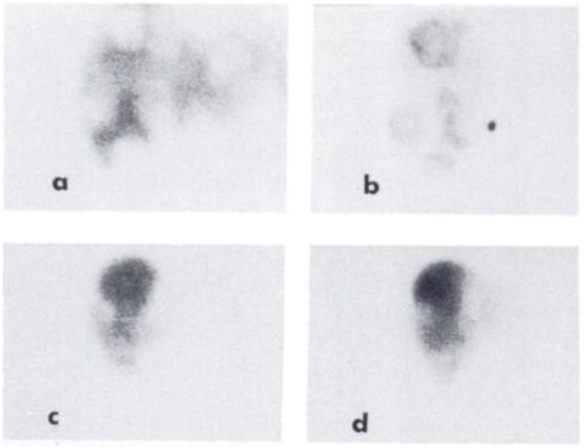

FIG. 1. Scintiphotos of liver, taken after i.v. injection of Tc-99m sulphur colloid (A & C) and after hepatic-artery infusion of Tc-99m macroaggregated albumin (B & D). A & B show preferential perfusion of tumor in right lobe, and C & D show poor perfusion of tumor throughout.

reduce the fraction of drug reaching the tumor. Such redistribution would not be detected by measurements of extrahepatic flow; studies of intrahepatic flow would be necessary.

Intrahepatic distribution could be measured at the same time as extrahepatic shunting, using serial infusions of Tc-99m MAA and DSM as described by Zeissman et al. Any major changes in the pattern of hepatic perfusion should be apparent on subtraction images of the liver. Zeissman et al. obtained images of the liver in the course of measuring extrahepatic shunting, but did not describe their findings in this regard.

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Reply

The purpose of our recent article (*1*) was to describe a quantitative method of calculating extrahepatic perfusion and A-V shunting to the lung using Tc-99m MAA hepatic-arterial perfusion scintigraphy (HAPS). In this study we demonstrated how this extrahepatic component changes with increasing doses of degradable starch microspheres (DSM), a new adjunctive agent for intraarterial chemotherapy. Extrahepatic flow can potentially result in less drug delivery to the tumor, with increased systemic exposure and potential toxicity. Drs. Valk, Guille, and Crea correctly point out that intrahepatic changes in blood flow away from the tumor towards uninvolved liver during starch administration

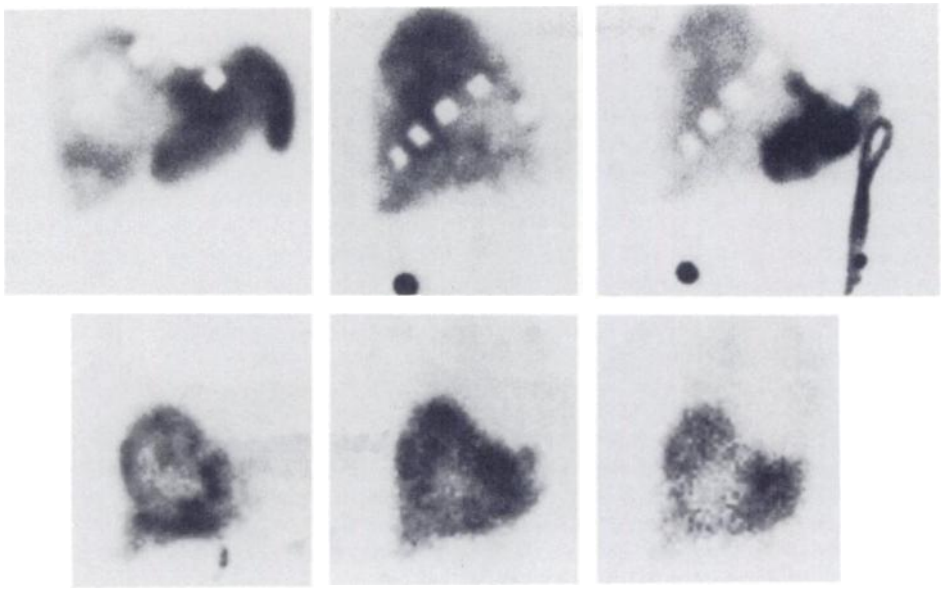

FIG. 1 Top left: Tc-SC liver-spleen scintiphoto in patient with colon cancer metastatic to liver. Top center: Patient has surgically placed catheter and subcutaneous infusion pump perfusing right lobe of liver as shown on this Tc-MAA HAPS study. Top right: Second percutaneously placed angiographic catheter is infused with Tc-MAA demonstrating perfusion of left lobe. Bottom left, center, right: Computer subtraction images of Tc-MAA perfusion images after first, third, and fifth injection of starch microspheres through surgically placed catheter, demonstrating change in perfusion pattern with increasing starch dosage. Progressive intrahepatic shunting of blood flow from right lobe to left lobe is seen.

could also adversely affect the benefit of the intraarterial approach to chemotherapy.

We have reviewed serial computer subtraction images (14 studies) in 12 patients who received increasing dosages of starch microspheres as described in our report, in order to evaluate possible resulting changes in intrahepatic perfusion. In nine studies no change in intrahepatic perfusion pattern was seen. Six of these patients received five consecutive injections, one patient received four injections, and two patients received three injections. The other five studies did show a change in intrahepatic perfusion with increasing doses of DSM. Two showed moderate (25-60%) changes in perfusion away from tumor areas after the fifth injection of starch microspheres. Only one had a major change in perfusion pattern (Fig. 1). The other two patients actually showed somewhat improved perfusion of the tumor areas after the first injection, compared with baseline. So major intrahepatic changes in perfusion away from tumor occurred infrequently in the dose range studied and usually with the larger doses of starch microspheres.

Since DSM temporarily block hepatic blood flow, it is not surprising that changes in intrahepatic and extrahepatic perfusion may result with increasing numbers of administered particles. Tc-99m MAA HAPS allows us to evaluate these potential changes qualitatively and quantitatively in order to safely apply new adjunctive forms of intraarterial chemotherapy.

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Tc-99m DMSA Uptake by Metastatic Carcinoma of the Prostate

Technetium-99m dimercaptosuccinic acid (Tc-99m DMSA) has a high affinity for renal cortex and is a very valuable agent for imaging of the renal parenchyma without interference from pelvicalyceal activity (*1*). Besides localization of Tc-99m DMSA within the normal renocortical tubules, there has been a report that

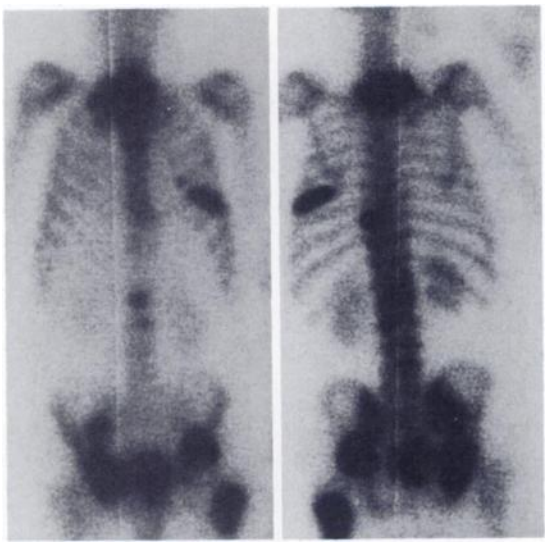

FIG. 1. Anterior (left) and posterior (right) total-body scintigrams performed 2½ hr after injection of Tc-99m MDP, showing multiple focal areas of increased activity in keeping with metastatic lesions in lower cervical spine, upper, mid, and lower thoracic spine, acetabular regions of pelvis bilaterally, right ilium, left intertrochanteric regions, and proximal shaft of left femur. No definite primary tumor was known at this stage.