Introduction

The results of hepatic resection for secondary liver tumours have (steadily) improved as a result of advances in surgical technique, perioperative management and diagnostic modalities which enable an earlier and more accurate detection of liver metastasis. Despite the development of extracorporeal liver surgery which enables the possibility of removing centrally located or multilocular intrahepatic tumours, only a small number of patients with secondary hepatic tumours are candidates for radical surgery. Liver transplantation has broadened the limits of potential radicality by removing the diseased liver in total. At the outset in the development of liver transplantation patients with otherwise unresectable hepatobiliary malignancies were thought to be almost ideal candidates for liver grafting due to their superior physical condition compared to patients suffering from end-stage liver disease and portal hypertension. Between 1968 and 1988 every fourth liver transplant in Europe was performed for hepatobiliary cancer. However, long-term results of liver transplantation for secondary hepatic tumours were disappointing since the vast majority of patients developed early tumour recurrence. With continuing improvements in immunosuppression and operative techniques, it is no longer the technical ability and expertise that determines long-term survival after liver transplantation but careful patient selection. Thus, the indication for liver transplantation in hepatobiliary malignancies, especially of secondary hepatic tumours, has become one of the most controversial issues in liver transplantation. This is reflected by the decreased frequency of liver transplantation for liver malignancies in the last decade. In the European Liver Transplant Registry (ELTR), a total of 16 414 liver transplantations were listed between January 1988 and December 1995 but only 11% (n = 1734) were performed for hepatobiliary cancer. Of these patients, only 9% underwent liver grafting for hepatic metastases (Table 8.1).

Although hepatic transplantation for metastases from a variety of primary tumours has been performed up until the present time, there are few conclusive data concerning the role of liver transplantation in the treatment of secondary liver tumours. In one of the first registry reports, Penn summarized data on 40 liver transplantations for various metastatic tumours including adenocarcinoma of the colon (n = 10), neuroendocrine tumours (n = 14), leiomyosarcoma (n = 5), carcinoma of the breast (n = 3) and each one of meningioma, neuroblastoma, renal cell carcinoma, cystosarcoma of the pancreas, seminoma and malignant melanoma as well as one haemangiopericytoma and one unknown primary tumour. In this heterogeneous group, eight patients survived for more than 24 months and only two patients survived longer than five years but with recurrent or...
residual tumour. A life table analysis of these data revealed an overall two-year survival rate of 38% and a five-year survival rate of 21%. The largest single center experience with liver transplantation for metastatic cancer was reported by Iwatsuki and his colleagues from Pittsburgh. Their series of 42 patients comprised 22 cases of neuroendocrine tumours, 12 adenocarcinomas, 7 malignant stromal tumours and 1 malignant melanoma. In 29 patients, the Pittsburgh group performed allografting with liver alone or combined with islet cells and in 13 cases as cluster transplantation (liver, pancreas, duodenum). Mortality at three months was 16.6% for the first group and 38.5% for the latter. Iwatsuki described a high tumour recurrence rate in all tumour groups within the first postoperative year. Most of these patients died within two years after liver grafting. However, they observed an overall tumour-free survival of 45% for neuroendocrine tumours.

These two series show that tumour recurrence is the rule but, on the other hand, it has to be appreciated that long term survival after liver transplantation has been observed in several different tumour types. This emphasizes the problematic nature of the indications for liver transplantation for metastatic disease. In oncologic surgery tumour recurrence and low survival rates are also frequent but there is less discussion regarding the justification of surgery if palliation, prolongation of life or only the hope for cure are possible. The same goals are true for liver transplantation but here the extremely high costs and the limitation of donor organs have to be taken into account. However, all these arguments become somewhat problematic if prolongation of life or at least a good quality of life can be achieved. A detailed analysis of the experience with liver transplantation in transplant centres across the world is presented in an attempt to address these various issues when liver grafting is considered for metastatic disease.

## Colorectal Metastases

In the early years of liver transplantation, irresectable colorectal metastases were by far the most frequent indication for secondary liver tumours. The largest single-centre experience was reported in 1987 by Mühlbacher and colleagues who grafted 9 patients with colorectal metastases. The overall one-year survival was 67% with 2 patients alive three years after transplantation and with one of them free of detectable tumour. Up until 1988, a total of 30 transplants for colorectal liver metastases had been performed in seven European centres. Only 6 patients were alive after two years and there was no five-year survivor. The longest reported survival after liver transplantation for colorectal metastases is four years and ten months. In Hannover 4 liver transplantations were performed for colorectal metastases with one of them being undertaken as an urgent transplantation after a failed attempt at extracorporeal liver resection; 2 out of the 4 patients died from septic complications, the other 2 patients died from tumour recurrence at 11 months and 32 months. Although tumour recurrence was noted frequently within the first postoperative year in both the Vienna and Hannover series a few patients remained completely free of symptoms for a considerable period of time. Quality of life was often excellent and even unaffected by recurrence for a period until patients finally had a rapid decline in their physical condition although they succumbed with large tumour loads.

## Metastases of Mesenchymal Tumours

Data on liver transplantation for metastatic mesenchymal tumours are uncommon. The Pittsburgh group reported 7 transplantations for metastatic malignant stromal tumours with 6 of these patients undergoing cluster transplantation. Despite a relatively high recurrence rate after liver transplantation, the authors suggested a more favourable course compared to metastases of epithelial origin. For the 6 patients undergoing cluster transplantation, the Pittsburgh group noted a recurrence rate of 83%. The incidence and median time of tumour related mortality was 66% (4 of 6 patients) and 938 days, respectively. At the time of reporting, 2 patients were alive at 19 months with recurrence and at 49 months apparently free of tumours. Similarly, Olthoff published a report of a single patient who underwent liver transplantation for irresectable metastases of a leiomyosarcoma of the stomach. This patient was alive 70 months after transplantation without evidence of disease.