# PILOT STUDY ON THE TREATMENT OF DIGESTIVE TUMOURS BY INTRA-DUCTAL HIGH-INTENSITY ULTRASOUND

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**Abstract**

Minimally invasive endoscopic treatment of cholangiocarcinoma by physical agents may be a good alternative when radical surgery is not possible. The objective of the study was to evaluate the clinical feasibility and short-term results of local tumour destruction with an intraductal high-intensity ultrasound probe. The applicator consisted in a flexible shaft ended by a flat water-cooled transducer (8 x 2.8 mm²) operating at 10 MHz. The treatment was applied to 10 patients. In one patient, histolopathologic assessment of the resected tumour revealed coagulation necrosis extending on a depth of 10 mm from the bile duct lumen. In the second operated patient, biopsies were negative in the treated zone. Permanent stent removal was possible in one patient after complete regression of the cholangiocarcinoma. A partial response was observed in 4 patients (Pre-treatment underestimation of the volume to be treated) and no response in 3 patients (bad acoustic coupling).

## Introduction

Digestive tumours have a very bad prognosis [1] for two main reasons: they are usually diagnosed very late and systemic treatments were demonstrated to have a small efficacy on these tumours. Although thermal ablation by High Intensity Focused Ultrasound (HIFU) becomes more and more accepted in neurology, ophthalmology and urology [2], this new therapeutic modality is not appropriate when treating these deep seated tumours unreachable from outside the body. In these cases, an interstitial approach is preferable. The method consists in driving through the body and positioning in contact to the targeted volume a miniature ultrasound applicator. Such an applicator was designed and used during a standard Endoscopic Retrograde Cholangio-Pancreatography (ERCP). This applicator was tested clinically on 10 patients. The objective of this study was to evaluate the clinical feasibility and short-term results of local tumour destruction with this applicator.

## Material

The active head of the applicator is a plane transducer which dimensions are 8 x 2.8 mm² (Figure 1). The transducer operates at a frequency of 10 MHz to favour heat deposition. Preliminary in vitro and in vivo studies demonstrated that coagulation necroses could develop over a depth of 10 mm with this frequency. Water-cooling of the external face of the air-backed transducer enables coupling with targeted tissues. A quasi transparent to ultrasound membrane is wrapped round the active head to seal the cooling system. Degassed water at ambient temperature runs along the transducer and drains in the bile duct lumen. The applicator (3.6 mm OD) fits inside the operating channel of a jumbo-duodenoscope (TJF-20, Olympus Optical Co., Ltd., Tokyo, Japan). The body of the applicator is made of overlapped coils in order to controlled remotely rotation of the active head. A 0.018 inch guidewire (Pathfinder, Boston Scientific, Natick, MA) fits inside the applicator to facilitate positioning of the transducer in the biliary stricture.

Figure 1: Active head of the applicator

## Methods

In order for a patient to be selected for the study, a malignant cancer of the duodenal papilla or a cholangiocarcinoma had to be diagnosed histo-pathologically. Patients operable for cure could be included too if the ultrasound therapy could be done one week before surgery. Patients presenting tumors developing in intra-hepatic ducts, high risk for general anesthesia, systemic infection, evidence of diffuse liver metastases or permanent coagulation deficiency were not involved in this pilot study. Enrollment was limited to 10 patients. This protocol was approved by the ethics committee of Cochin Hospital (Paris, France).

Treatment was performed during standard ERCP. The applicator was positioned under fluoroscopic guidance (Figure 2). Twenty elementary exposures were performed to cover 360 degrees. The ultrasound intensity was set to 14W/cm². The first exposure lasted 20 s and each of the following 10 s. the transducer was rotated manually through an angle of 18° between exposures. After treatment, 11.5F Amsterdam-type stent(s) was left in situ until the time of planned follow up evaluations.

Follow up sessions were scheduled for 3 and 6 months after ultrasound therapy. Further follow up was continued by quarterly telephone inquiry with the patient and primary care physician for up to 2 years after treatment.

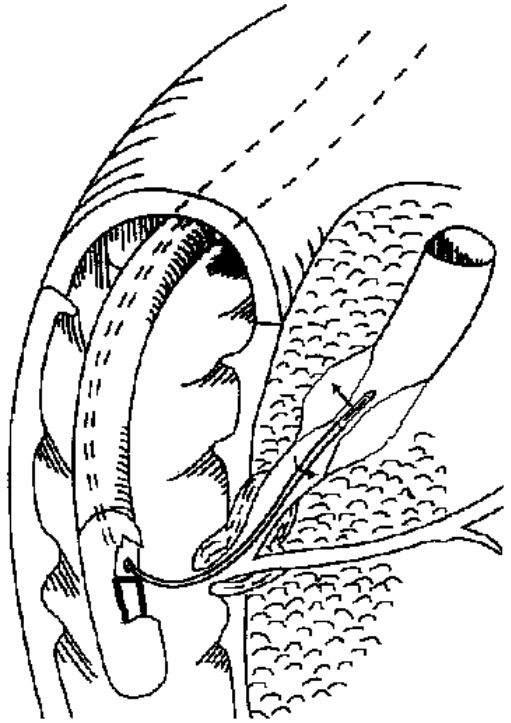

Figure 2: The ultrasound applicator was positioned in the bile duct in front of the tumor to be treated

**Results**

Lesions treated included carcinomas of the papilla (3 cases), bile duct cholangiocarcinomas (2), Bismuth grade I and II hilar cholangiocarcinomas (4), and intra-hepatic cystadenocarcinoma (1). Two patients underwent surgery within a week after ultrasound treatment.

No serious adverse effects were observed. However, one patient who required trans-hepatic drainage developed right upper abdominal pain for 12 hours. This was rather due to intraperitenoal leakage of bile than ultrasound treatment. In one patient who underwent post-ultrasound surgery, histopathologic examination of the resected tumour revealed extensive coagulation necrosis up to 10 mm in depth surrounding the bile duct lumen. In the other operated patient, biopsies in the treated portion of the bile duct were negative for malignancy. A complete regression of cholangiocarcinoma was observed in one patient, allowing for permanent stent removal (Figure3). Four patients presented partial responses to treatment with local regression of the tumours but distal proliferation. In one case, before treatment, no stent could remain patent for more than 4 weeks. Immediately after treatment, jaundice decreased and no further stent occlusion occurred until death 5 months later. No response was observed in 3 patients. Cancers of the duodenal papilla were diagnosed to these 3 patients.

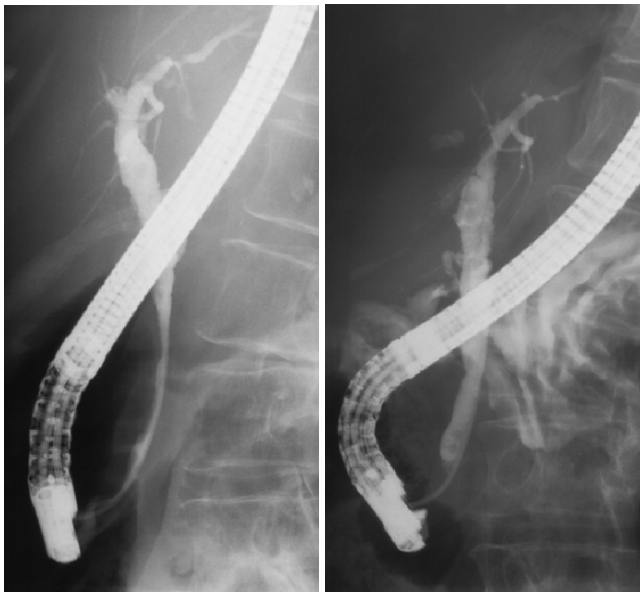

Figure 3: The bile duct stricture disappeared after high intensity ultrasound treatment in one case: fluoroscopic images before treatment (left), after treatment (right)

**Discussion and conclusion**

This work demonstrated that digestive tumours can be treated by high-intensity ultrasound using an endoscopic approach. The treatment was not invasive at all. Ultrasound therapies were performed in about 30 minutes and anaesthesias were just a little bit lengthened. Follow up sessions corresponds to normal visits for stents replacements.

Even though the choice of a tubular transducer could seem simpler for achieving cylindrical zone of coagulation, we demonstrated in earlier work [3] that a plan transducer allows for deeper and quicker heating. Coagulation necroses over a depth of 10 mm were obtained in 10 s. This exposure duration can be considered almost independent to perfusion. This therapeutic depth corresponds very well to the infiltration of these digestive tumours.

Partial responses to treatment were most of the time due to underestimation of tumour extent before ultrasound therapy. When acoustic coupling was

deficient, no response to treatment was observed. This was especially true for cancers of duodenal papilla where strictures are not as tight.

Now that we have demonstrated the efficacy of this method, we could easily apply it for the treatment of others tumours. This method is of particular interest when it comes to treat sector-based cancers, covering only part of an organ lumen [4].

In order to reduce uncertainties on transducer positioning, we also designed a cylindrical array for electronic creation and rotation of a plane wave [5].

Preliminary results for treating these tumours with an extremely bad prognosis are very satisfactory. One patient was considered to be cured. But Longer-term follow-up and another pilot study will confirm whether this method is curative in some cases and if it can reduce the need for biliary stent placement.

**References**

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