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Bloodless hepatic resection with automatic bipolar radiofrequency generator and multielectrode device

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Abstract
Liver resection is a standard treatment for liver tumours. Intra-operative blood loss remains a major concern during liver resection due to its association with higher postoperative complications and shorter long-term survival. To perform bloodless hepatic resection we realized an apparatus consisting of an incremental, bipolar radiofrequency generator and a probe with six in-line needles (SURTRON SB). Several ex-vivo and in-vivo pig liver experiments and a first-phase clinical study allowed the realization of a prototype radiofrequency (RF) generator that works at 470 kHz, 150 watts maximum power delivered. The probe consists of six needle electrodes of 1.5 mm diameter, with 4.5 mm free space, 6.0 mm centre to centre, between each. We obtained a coagulation of 35 mm length and 12 mm width. The transection was performed with a common scalpel after coagulation of liver parenchyma. We observed good healing of the liver edge both in animal model and in ongoing pilot clinical study. Coagulation with SURTRON SB allows a feasible, easy and safe bloodless liver resection. This method is tolerated with no systemic complication or adverse reaction. This technique offers a method for a bloodless hepatic transection without the need for sutures, ties, staples or tissue glue.

Key words: Hepatic tumours, liver resection, incremental, bipolar radiofrequency

Introduction
Hepatic resection is currently considered the gold standard for the treatment of primary and secondary liver tumours. Progress in surgical techniques, anaesthesia, anatomy and hepatic physiology knowledge allows feasible and safe liver surgery.

Intra-operative blood loss remains a major concern during liver resection due to its association with higher postoperative complications and shorter long-term survival (1,2). To reduce blood loss during hepatic resection several vascular control manoeuvres, both surgical and pharmacological, can be performed (Pringle’s manoeuvre; totally vascular exclusion) (3,4). To minimize intra-operative blood loss several tools have been developed during recent years, and many studies have been performed to compare this instrument with standard clamp crushing (5–12).

In 2002 Habib described an innovative technique with monopolar radiofrequency (RF) to perform blood-less wedge resection without the need for sutures, ties, staples, or tissue glue (13). This technique makes it possible to coagulate liver parenchyma around the tumour with a monopolar cooled tip to obtain the closure of haematic and biliary structures on the resection plane (13). Consequently, in 2004, the same author described a major hepatic resection without vascular control using the same technique (14).

After experience in monopolar radiofrequency ablation of liver tumours (15–17) we started research in the field of bipolar radiofrequency, primarily focused on tumour ablation, and then on liver resection, in collaboration with engineers working at the Laboratory for Electronic Design (LED) Spa, Aprilia (Latina) Italy.

In this paper we describe the experimental route followed to realize a bipolar, incremental radio-frequency generator (SURTRON SB) and a probe...
with six in-line needles (electrodes), which is intended to achieve coagulative ablation in a plane which can then be cut through with a scalpel.

Materials and methods

From January 2003 several experimental procedures were performed on *ex-vivo* pig livers, at the Department of Biology, Animal Facility Centre (STA) University of Rome Tor Vergata. In these procedures an RF electrosurgical apparatus in bipolar mode was used to produce a sinusoidal pure wave of 660 kHz frequency, 140 V output, and maximum power of 30 W, with 100 Ohm impedance that fed two electrodes (needles). The entire system was originally composed of three RF generators and six electrodes. Finally, we realized a single generator which was modified to deliver 60 W, through six electrodes with 500 Ohm impedance, and forced cooling. The apparatus was modified in order to supply controlled power simultaneously to five bipolar circuits through the six electrodes that constituted the application tool, fed from an output transformer with six terminals. The following parameters were evaluated:

- Distance between electrodes,
- energy delivered,
- width and thickness of necrosis, and
- needle diameter.

During the *ex-vivo* and early *in-vivo* phases, the evaluation of necrosis entity was determined by experimenters only by naked eye. During coagulation we observed that current flow initially grew, and then decreased because of tissue desiccation. Delivery of energy was stopped when experimenters judged that full necrosis had occurred. The impedance and current at that moment were noted and then engineers were able to realize automation based on these parameters. Delivered energy is regulated automatically according to tissue impedance between the two central electrodes, and is related to tissue thickness. This algorithm allows each electrode to be shut down when current flow drops to 50% of the previous maximum level, the value determined by repeated observation of events when under manual operation.

After approval from the Animal Ethics Committee, 18 liver resections on six pigs (Landrace pig) were performed from September 2003 to December 2004. All procedures were performed under general anaesthesia, with tracheal intubation and continuous cardiac monitoring, with midline laparotomy and without vascular control. Nine atypical liver resections were performed in three animals sacrificed at the end of the experiments. Nine atypical liver resections were performed in three animals, at two different times. The animals were kept alive after the first operation to evaluate the principal complications (bleeding, biliary leakage). Blood sampling was performed before the first operation and on the fourth post-operative day to assess bleeding. During the second operation, we carefully evaluated the entire abdominal cavity and the liver edge, performed biopsy of the necrotic tissue (for histological control) and carried out another two resections upon each animal.

The resections were performed with a normal scalpel after multiple application of the multi-electrode probe along the established line (Figure 1). To obtain optimal coagulation of the slice of liver parenchyma, and to facilitate the cutting of the tissue, we decided to perform a double parallel line of application of the probe. During this phase we used an original incremental generator with 475 kHz, 160 Volts and 150 Watts (SURTRON SB) (Figure 2), as explained in the technical detail section.

Finally, to assess the tolerability and safety of the system on human beings, after IRB approval, we designed, and are currently realizing, a clinical pilot study at our department.

Technical details

The schematic set-up for the SURTRON SB (Figure 3) consists of a radio frequency generator whose main characteristics are listed in Table I. Most of the well-known difficulties associated with the implementation of thermo-coagulation through
the use of radio-frequency electrode vectors inserted in order to coagulate the parenchyma derive from:

- Desiccation as a result of the high density of current around the electrode in contrast to the progress of coagulation in the surrounding areas,
- the adhesion of electrodes to the tissue due to coagulative necrosis and consequent difficulties in retracting them at the end of treatment.

In the multi-electrode set-up traditionally used, in which the probe resembles a "comb" and has access to the same lines, the electrodes are fed in such a way that adjacent electrodes are connected to the opposite poles of the generator. There is, therefore, a convergence of electro-surgical currents created in adjacent electrodes through the tissue interposed by them that, consequently, flows through the electrodes (Figure 4).

For the purpose of limiting the drawbacks described above, a radiofrequency generator has been developed that has the capability of feeding the electrodes so that the difference, not the sum, of current flowing through the tissue outlined by

<table>
<thead>
<tr>
<th>Table I. RF generator characteristics.</th>
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<tbody>
<tr>
<td>FREQUENCY=470 kHz</td>
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<tr>
<td>OUTPUT POWER=150 W</td>
</tr>
<tr>
<td>LOAD IMPEDANCE=250 Ω</td>
</tr>
<tr>
<td>OUTPUT POWER LEVELS=10</td>
</tr>
<tr>
<td>OUTPUT CHANNELS=6</td>
</tr>
<tr>
<td>INCREMENTAL VOLTAGE=70 V</td>
</tr>
</tbody>
</table>

Figure 2. Surtron SB.

Figure 3. Surtron SB electronic diagram.

Figure 4. Standard multi-electrode power supply electronic scheme.
electrodes and those adjacent converge in each intermediate electrode. What has been obtained by supplying the electrodes in this way is that each of them receives a voltage higher than the preceding one in the sequence (incremental mode) (Figure 5).

In this way, the current flows in the farthest electrodes and in all impedance of the portion of tissue comprised among the electrodes, while there is no current in the intermediate electrodes. The most accentuated heating in the vicinity of the farthest electrodes determines the priority for coagulation and desiccation for those electrodes. The current that is impeded in continuing its flow through the farthest electrodes transfers primarily to the adjacent electrodes and, once desiccation around the new pair occurs, to the more internal ones until the treatment is complete. Although the system used to feed the electrodes reduces the chances of premature desiccation within the probe electrodes, especially internal ones, excessive adhesion of the electrodes to the coagulated tissue continues to persist, thus necessitating additional features in an attempt to eliminate this problem. For this purpose, the electrodes have been coated with an anti-adhesive shield that consists of different successive layers of NbN and CrN. By reducing adhesion of electrodes to coagulated tissue and, in any event, to avoid burning, automatic interruption of the current to electrodes is provided when desiccation around the electrode begins following coagulation. The progression of the current distributed to each of the six electrodes of the probe comb inserted into the parenchyma is continuously monitored through a micro-controller programmed to determine the detachment of each electrode when indicated by a substantial increase in impedance. Our experiments have indicated that the separation of an electrode should occur when there is a reduction of current flow to 50% of the maximum value reached. The device also includes automatic setting of treatment power level. The impedance of the parenchyma is measured at the beginning of the coagulation process and the appropriate power is calculated. Following each electrode detachment, the power is readjusted to supply the correct current to flow.

Supplying the electrodes through the use of this bipolar modality allows the device to function with relatively low voltage levels produced by the generator, typically inferior to 100 Vpp between the pair of electrodes, so that the moderate electromagnetic field induced is, at its highest levels, less than 20V/m when measured at a distance of 15 cm from the probe. This reduces the potential risk of damage due to the dispersion of radio frequency current, not only for patients but also for surgeons and support staff present in the operating theatre.

The device is completed by two accessories which have proven to be very useful during the operating surgical treatment:

- An easy-to-operate guide designed to maintain the parallel position of the electrodes and to avoid their bending during insertion into the parenchyma, thereby preventing the relative distance between the pairs of adjacent electrodes from being modified (Figure 6), and
- a protective device which protects the surgeon’s hand and surrounding organs from accidental damage during use of the probe and thermally insulating tissue below the parenchyma during coagulation treatment (Figure 7).

Results

Schematically, we can summarize the results as follows.

From the *ex-vivo* experiments we can state that:

- Power delivered and distance between electrodes to obtain homogeneous necrosis are correlated in an inversely proportional manner; in fact, by reducing the power supply it is possible to space out the electrodes. This causes lengthening of the period of power output and a significant increase
in the volume of necrosis obtained (also in the transversal plane).

- The maximum distance between two adjacent electrodes, such as to allow homogeneous coagulative necrosis in the hepatic tissue, is 1.5 cm.
- The needle calibre chosen is 1.5 mm; finer needles are unable to maintain a correct direction during their passage through the parenchyma.
- Needles are not insulated and consequently the necrosis was of full thickness (Table II).

After these results, combs with diameters of 1.5 mm and 1 mm and spaced at 6 mm, 8 mm, and 1 cm were studied on \textit{in-vivo} pig liver.

Data obtained on the first pig showed that distances > 6 mm did not result in homogeneous necrosis; at a power of 30 W, the current was not able to propagate between adjacent electrodes, and increased power caused charring around the needle that increased the impedance. This, in turn, impeded propagation of current.

It was also noted that needles of too small a calibre tended to deflect and therefore, from that point, the prototype used adopted a group of six needles of 1.5 mm, at 6.0 mm intervals.

From the \textit{in vivo} experiments we verified the following:

- In liver resections obtained with a single line of probe application, a good parenchyma coagulation and a good blood vessel sealing (up to 4.5 mm diameter) were obtained. During transection with a common scalpel it can be difficult to remain along the correct coagulation plane, with consequent bleeding from parenchyma not well coagulated and the need for stitches. Therefore, after a double line of coagulation, we never had this kind of problem.
- With the first application of the probe we obtain a slice of 12 mm of necrotic parenchyma, 6 mm on each side of the needles. The second application on the edge of the first coagulated tissue produces a further necrosis of 6 mm. We transect along the second needle line, leaving a slice of about 1 cm of necrotic tissue \textit{in situ} (Figure 8).

<table>
<thead>
<tr>
<th>Needle diameter</th>
<th>Distance between electrodes</th>
<th>Treatment duration</th>
<th>Power (Watts)</th>
<th>Thickness</th>
<th>Width</th>
</tr>
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<tbody>
<tr>
<td>1.5 mm</td>
<td>15 mm</td>
<td>10 minutes</td>
<td>30 W</td>
<td>1–3 cm</td>
<td>15 mm</td>
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<tr>
<td>1 mm</td>
<td>15 mm</td>
<td>10 minutes</td>
<td>30 W</td>
<td>1–3 cm</td>
<td>15 mm</td>
</tr>
<tr>
<td>1.5 mm</td>
<td>10 mm</td>
<td>7.5 min approx</td>
<td>30 W</td>
<td>1–3 cm</td>
<td>12 mm</td>
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<tr>
<td>1 mm</td>
<td>10 mm</td>
<td>7.5 min approx</td>
<td>30 W</td>
<td>1–3 cm</td>
<td>12 mm</td>
</tr>
<tr>
<td>1.5 mm</td>
<td>6 mm</td>
<td>3.5 min approx</td>
<td>30 W</td>
<td>1–2.5 cm</td>
<td>9 mm</td>
</tr>
<tr>
<td>1 mm</td>
<td>6 mm</td>
<td>3.5 min approx</td>
<td>30 W</td>
<td>1–2.5 cm</td>
<td>9 mm</td>
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<tr>
<td>1 mm</td>
<td>6 mm</td>
<td>3.5 min approx</td>
<td>40 W</td>
<td>2.5–3.5 cm</td>
<td>9 mm</td>
</tr>
<tr>
<td>1 mm</td>
<td>6 mm</td>
<td>3.5 min approx</td>
<td>60 W</td>
<td>3–4 cm</td>
<td>9 mm</td>
</tr>
<tr>
<td>1 mm</td>
<td>6 mm</td>
<td>2.5 min approx</td>
<td>60 W</td>
<td>2.5–3.5 cm</td>
<td>9 mm</td>
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Table II. Summarized data obtained in \textit{ex-vivo} experiments with various calibres of needle, power and distance.
• Using the double line method, the haemostasis is optimal and it is not necessary to apply stitches to the parenchyma.
• The application time for in-vivo experiments depends on blood-flow abstraction of heat. Without vascular control the first needle line application requires about 4–5 minutes and the second requires about two minutes (average half time). Vascular control notably reduces coagulation time.
• No animals kept alive after the first operation died, all of them resuming normal activity on the second look. In addition, we observed very strong adhesion between the transected liver and stomach.

Discussion

When appropriate, liver resection is the gold standard for the treatment of liver tumours. The major technical challenge in liver resection is the control of bleeding during transection of the liver parenchyma. Intra-operative blood loss remains a major concern during liver resection due to its association with higher postoperative complications and reduced long-term survival. Many experimental and clinical studies have shown that blood transfusions, possibly due to modulation of the immune function, have an adverse effect on postoperative outcome after surgery for malignant neoplasms (2).

Surgical techniques and the efforts to reduce intra-operative blood-loss both developed at the same time. Maintenance of central venous pressure < 4 mmHg (hypotensive anaesthesia) can help reduce blood loss during heptectomy, shorten the length of hospital stay, and has no detrimental effects on hepatic or renal function (3). Various techniques of hepatic vascular control have been tested, from Pringle’s manoeuvre to total hepatic vascular exclusion (4,5).

To minimize bleeding and to simplify surgery, several devices have been developed during recent years (CUSA, Ligasure, Hydrojet, Harmonic scalpel, Argon Beam, tissue link), but crush technique is still appropriate (6–12). Therefore, the optimal method of liver parenchymal resection to obtain minimal blood loss remains to be established, and currently the choice of technique depends largely on the individual surgeon’s preferences (10).

RFA has been widely used for the destruction of unresectable tumours where the ablated tissue remains in situ without detrimental effects. Habib introduced monopolar radiofrequency techniques into hepatic surgery in 2002, evaluating the role of this method in minor hepatic resection. He described how radiofrequency energy was applied along the margins of the tumour to create “zones of necrosis” prior to resection with a common scalpel. He concluded that wedge, segmental, and major hepatic resection assisted by radiofrequency were safe and offer a new method for transfusion-free resection (13,18,19).

Gananadha and Morris realized a prototype device with 11 electrodes connected to a radio-frequency generator (RITA 1500). It works in a bipolar fashion with the aim to realize a plane of ablation of the liver parenchyma. They compare resections using the ultrasonic aspirator (UA) and using the Kelly clamp with and without preliminary RFA. Bleeding reduction was observed using RFA before the resection (20). In a similar experimental design, studies were carried out on liver resections in five sheep using a device with six needles (21). Finally, they tested the technique with anatomical resection in eight patients. Half of the resection plane was made with Ultrasonic Aspirator (UA) after inline radiofrequency ablation (ILRFA), and half with UA alone. The difference in blood loss was statistically significant (22).

We realized a system consisting of a radio-frequency generator and a multi-electrode probe, which works in a bipolar fashion. Each application of the device produced a “slice” of coagulative desiccation of the whole thickness of the parenchyma, with a mean of 3.5 cm length and a mean 1.2 cm width. Data from experiments in animal models have confirmed this pattern of necrosis. Coagulation of the liver parenchyma is tolerated by animals with no systemic complications or adverse reactions. The double-line coagulation technique allows much safer transection with a scalpel and seals vessels greater in diameter without the necessity of stitches.

Our generator is specifically designed to service this technique and, following a series of improvements, it is now able to check and control the impedance before delivering energy and then to automatically choose the correct power output. Furthermore, this generator automatically shuts down each electrode when desiccation is reached. The probe is relatively manageable; a specific protective device gives thermal protection to the surgeon’s hand and surrounding organs. Thanks to the necrosis, we expected lower recurrence on the liver edge as a long-term result.

To access the tolerability and safety of the system on human beings, after IRB approval, we designed and are currently realizing a clinical pilot study in our institution. Early results are close to the
experimental data. Moreover, we recently performed two polar kidney resections in a pig model with good coagulation of the parenchyma, both with and without vascular control. Therefore, we are encouraged to continue in this way in order to evaluate coagulation in organs other than liver, and also to investigate the laparoscopic application of this system.

References