Argon and helium plasma coagulation of porcine liver tissue

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Abstract

Objective: Argon plasma coagulation (APC) and helium plasma coagulation (HPC) are electrosurgical techniques that provide noncontact monopolar electrothermal haemostasis. Although these techniques have been widely used clinically during the last three decades, their in vivo effects on liver tissue remain unclear.

Methods: We investigated the effects of different power levels (10–100 W) of APC and HPC on liver coagulation in 11 Landrace pigs. Capillary blood flow and capillary blood flow velocity were recorded with a combined laser Doppler flowmeter and spectrophotometer. The temperature, clinical biochemical parameters, blood gas parameters, bile duct-sealing effect, and coagulation depth were measured.

Results: APC and HPC significantly reduced the capillary blood flow and capillary blood flow velocity compared with baseline flow. No significant temperature change was measured on the liver surface immediately after coagulation. The clinical biochemical and blood gas parameters were not different before and after coagulation. The coagulation depth was positively correlated with the device power setting.

Conclusions: These results prove that APC and HPC provide sufficient superficial haemostasis. No significant systemic effects occurred following coagulation. The depth of the coagulation effect can be controlled through selection of the output power level.

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Introduction

Argon plasma coagulation (APC) is a non-contact electrosurgical technique that has been widely used in open surgery for the last three decades. Endoscopic application of APC has been available for about

15 years.[1–3] In both open and laparoscopic abdominal surgery, APC is mainly used to establish secondary haemostasis after resection of parenchymal organs, predominantly the liver, spleen, and kidney.[4–6] Another important application is the endoscopic use of APC in the palliation of obstructive tumour growth in the oesophagus, stomach, or intestine[7]; the treatment of oesophageal tumours[8]; and the coagulation of angiodysplastic transformations in the stomach or intestine.[9] The use of APC in dermatology has also been described.[1] Plasma coagulation is another form of radiofrequency electrocautery, delivering electrical energy to tissue through a jet of ionised argon gas and thus providing monopolar electrothermal haemostasis. Because the electrical energy is delivered through the arc of ionised gas, it is a noncontact technique with the advantage of preventing the coagulated tissue from sticking on the electrode.[10] The plasma beam, which is ionised in the electrical field between the electrode and tissue, is automatically directed to the area of the lowest electrical resistance. Because the resistance in this area rises due to increasing desiccation during the coagulation process, the argon beam automatically turns away to other areas not yet desiccated (where the electrical resistance is lower), producing a uniform limited depth of coagulation.[11,12] In liver surgery, several methods (clamp-crush technique, use of the Cavitron ultrasonic surgical aspirator, and use of a radiofrequency dissecting sealer) have been established for parenchymal transection and experimentally evaluated in terms of achieving primary haemostasis.[13] Plasma coagulation is mainly used for secondary haemostasis of large liver cut surfaces after resection to prevent secondary haemorrhage at a later stage.[14] Factors influencing the tissue effect are the duration of the application, the power setting of the device, and the distance from the probe to the tissue.[1] Despite the widespread clinical use of APC, its effects on liver tissue in vivo remain unclear because most clinical studies have focused on clinical outcomes rather than histological and functional examination findings.[14–16] Experimental studies have mostly concentrated on in vitro investigations.[1] A new technology was recently developed by Söring GmbH (Quickborn, Germany) in which electrical energy is delivered to tissue through a beam of helium instead of argon gas, providing a lower plasma temperature. This device is called a cold plasma coagulator (CPC); this should not be mistaken for cold atmospheric plasma, which is mainly used in the medical field for its antimicrobial activity.[17] Therefore, we termed this technique helium plasma coagulation (HPC) for clarification. To date, only one previous study (an in-vivo liver model) has compared APC with other coagulation techniques in terms of the coagulation depth,[18] and helium and argon have only been compared in the gynaecological setting with different application devices.[19]

The present study was performed to investigate the effects of two different carrier gases (argon and helium) during plasma coagulation of porcine liver tissue in vivo for the first time. It is also the first scientific evaluation of the CPC-1000 device (Söring GmbH Medizintechnik, Quickborn, Germany) used with helium as the carrier gas. The parameters analysed in this study were microcirculation, temperature, clinical biochemical parameters, blood gas parameters, bile duct-sealing effect, and coagulation depth.

Methods

All experiments were conducted in accordance with the national legislation governing animal studies. The Principles of Laboratory Animal Care (NIH publication 85-23, revised 2011) were followed. Official permission was granted from the

governmental animal care and use office. Eleven female Landrace pigs obtained from a disease-free barrier breeding facility were housed in open cages and allowed to acclimate to their surroundings for at least 1 week before surgery was performed. The pigs, weighing 27.5 ± 4.7 kg (mean $\pm$ standard deviation), were fasted 24 h prior to the experiments with free access to water. Of these animals, six were allocated to the APC group and five were allocated to the HPC group. The animals were treated similarly with the exception of the different carrier gases.

Surgery and recording of baseline values

The abdominal cavity was approached via a midline laparotomy. The baseline temperature and temperature after coagulation was measured at predetermined locations on the liver surface using a touchless standard infrared thermometer (VOLTCRAFT IR 260-8 S Infrared Thermometer; Conrad Electronics, Hirschau, Germany). At the same locations, the microcirculation was quantified using a combined laser Doppler flowmeter and spectrophotometer system (O2C [oxygen-to-see] system; LEA Medizintechnik, Gießen, Germany). The temperature during coagulation was measured with a thermographic camera (VarioCAM HD head 820; Jenoptik, ESW GmbH, Jena, Germany) on the ex-vivo liver surface for APC and HPC. This examination was performed at diverse device output power settings ranging from 10 W to 100 W in different areas. The infrared detector enables acquisition of infrared sequences with a spatial resolution of 1024×768 pixels with a temperature resolution better than 0.05 K. The camera was connected to a notebook via Gigabit Ethernet. Image sequences of 2-min length were recorded and analysed post-hoc using the IRBIS 3 plus software package (Infratec GmbH, Dresden, Germany).

Plasma coagulation

The device used was the CPC-1000 (Söring), which can be operated with either argon or helium. In the APC group, the liver surface was coagulated using argon gas with eight ascending device power levels (10 W, 15 W, 20 W, 25 W, 30 W, 50 W, 75 W, and 100 W). Measurement of the bile duct-sealing effect was performed at 40 W. A titanium mould with a square aperture of 1×1 cm was laid on the organ surface to standardise the coagulated area. Coagulation was performed for 5 s with a probe distance of 1 cm from the tissue at two locations on the left liver lobe. In the HPC group, helium was used to perform the same coagulations at identical power levels. Immediately after every coagulation process, the temperature and microcirculation were measured.

Noninvasive measurement of microcirculation

A combined laser Doppler flowmeter and spectrophotometer, the O2C system, was used in this study to noninvasively quantify the microcirculation at an 8-mm tissue depth. The O2C system is commonly used in various surgical disciplines.[20–24] The capillary blood flow and capillary blood flow velocity were recorded. To minimise the effects of regional blood flow variations, measurements were performed at two locations for each power level of the coagulator devices.

Histological examination

Two liver tissue specimens were collected for each power level of the plasma coagulator devices. The sections were fixed with neutral 10% buffered formalin and embedded in paraffin. Haematoxylin and eosin staining was applied. The depth of necrosis due to coagulation was measured in micrometres after calibration with an object micrometre.

Burst pressure (ex-vivo measurement)

Like fibrin sealants, is technically impossible for plasma coagulators to seal larger blood vessels; such sealing is normally performed as primary haemostasis during resection. Nevertheless, the aim of this study was to compare two techniques for secondary haemostasis. Therefore, burst pressure measurements were carried out in the bile duct system. This technique was previously described by Erdogan et al.,[25] who conducted burst pressure measurements in perfused organs. To exclude blood pressure-related effects, we performed the experiments ex vivo. In brief, all ligamentous connections to the liver were divided and the hepatic pedicle was isolated. Half of the left medial lobe was resected using a sharp scissors. The cut surface was either coagulated with an argon or helium beamer or sprayed with a liquid fibrin sealant (TISSEEL; Baxter Deutschland GmbH, Unterschleißheim, Germany) according to the manufacturer's specifications. The whole liver was retrieved after the animals were killed, and saline was continuously infused through the catheter in the common bile duct with an automatic pump system (Perfusor; B. Braun Melsungen AG, Melsungen, Germany). The pressure in the biliary system was recorded using a pressure monitoring system (Digital Pressure Meter, GMH 3161-13; Greisinger Electronic GmbH, Regenstauf, Germany). The cut surface was examined for leakage, and the maximum pressure achieved until leakage occurred was documented.

Statistics

All data are presented as mean ± standard deviation. Statistical analysis was performed using one-way analysis of variance with Bonferroni's post-hoc test or a nonparametric test (Mann–Whitney U test) with Prism 5.02 (GraphPad, La Jolla, CA, USA).

A P-value of <0.05 was considered statistically significant.

Results

Capillary blood flow (Figure 1)

At the lowest power level of 10 W, a reduction in the capillary blood flow to $47.9\% \pm 6.6\%$ of baseline flow for the APC device and to $59.1\% \pm 15.6\%$ for the HPC device was detected, achieving a significant reduction in capillary blood flow with both coagulator devices. These results were concordant with the clinical impression of complete haemostasis at the coagulated sites. The capillary blood flow was further reduced with ascending power levels (until the maximum level of 100 W). At the power level of 100 W, the capillary blood flow was reduced to $19.1\% \pm 5.6\%$ (APC) and $10.4\% \pm 2.7\%$ (HPC) of baseline flow. These values were the minimum flow values reached for both devices. At every power level, the reduction in baseline flow was significantly reduced with both the argon and helium plasma coagulators.

Capillary blood flow velocity (Figure 2)

Likewise, the capillary blood flow velocity decreased with rising coagulator device power levels, beginning with a reduction to $84.5\% \pm 8.6\%$ (APC) and $76.3\% \pm 6.4\%$ (HPC) at 10 W. The capillary blood flow velocity continued to decrease with ascending power levels. At 100 W, the maximum reduction in capillary blood flow velocity was reached at $62.7\% \pm 3.1\%$ for the APC device and $57.5\% \pm 5.5\%$ for the HPC device. The reduction in blood flow velocity was significantly reduced from 20 W onward. The reduction in capillary blood flow velocity with ascending coagulator device power levels was not as distinct as the reduction in capillary blood flow.
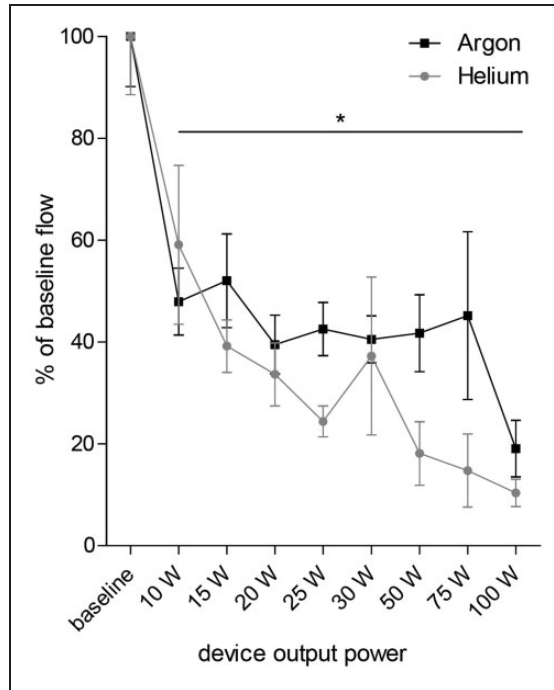
Figure 1. Capillary blood flow on the liver surface as measured with the O2C device. Data are expressed as percentage of baseline flow before coagulation. Data are shown as mean ± standard deviation; *$P < 0.05$ compared with baseline flow.

Temperature (Figure 3)

The baseline organ surface temperature was 32.4°C ± 2.3°C in the APC group and 33.6°C ± 1.8°C in the HPC group. Only marginal changes occurred following APC and HPC as measured with the infrared thermometer. Thermographic camera measurements during coagulation showed no difference at 40 W, while at 100 W, a lower mean temperature was recorded with HPC than APC (−1.53°C, $P = 0.0062$).

Clinical chemistry, haematology, and blood gas analysis (Table 1)

The clinical chemistry parameters (sodium, potassium, chloride, creatinine, urea, alanine aminotransferase, aspartate aminotransferase, glutamate dehydrogenase, Quick,

international normalised ratio, and activated partial thromboplastin time), white blood cells, red blood cells, and blood gas analysis values did not differ significantly before and after coagulation for both APC and CPC. Additionally, no intergroup differences were noted (APC vs. HPC pre-coagulation, APC vs. HPC post-coagulation).

Coagulation depth (Figures 4 and 5)

In the histological specimens, the coagulation zone was sharply distinguished from the vital liver tissue. The zone of necrosis showed a loss of hepatocyte features, leaving eosinophilic remnants of the hepatocyte cords with shrunken cytoplasm and occasional pyknotic hepatocyte nuclei as well as intercellular vacuoles and slight
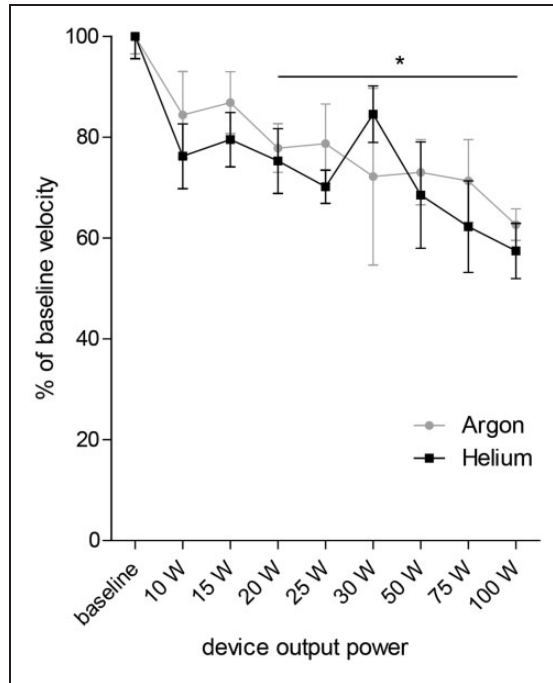
Figure 2. Capillary blood flow velocity on the liver surface as measured with the O2C device. Data are expressed as percentage of baseline flow before coagulation. Data are shown as mean $\pm$ standard deviation; *$P < 0.05$ compared with baseline flow.

haemorrhage. With ascending coagulator device power levels, the coagulation depth increased for both APC and HPC. The maximum coagulation depth at 100 W was $297 \pm 105\,\mu m$ for APC and $413 \pm 161\,\mu m$ for HPC. Linear regression showed $r^2 = 0.23$ for APC and $r^2 = 0.4$ for HPC. We found no distraction of the plasma beam to the mould, which was histologically proven by a uniform coagulation depth even at the margin of the coagulated sites.

Burst pressure (Figure 6)

No significant difference in the burst pressure was noted among APC (1003 ± 554 mmHg), HPC (1254 ± 579 mmHg), and use of the liquid fibrin sealant (TISSEEL) (1500 mmHg; maximum value at all recordings).

Discussion

Plasma coagulation has been used in a variety of clinical fields. It has become an important tool in interventional endoscopy.[7,9,26–28] Due to its property of automatically turning away from already desiccated, coagulated sites, plasma coagulation produces a uniform and limited depth of coagulation; therefore, it can be used on thin-walled regions in the gastrointestinal tract.[29] The clamp-crush technique has been indicated as the method of choice for parenchymal transection in liver surgery, although other methods (use of the Cavitron ultrasonic surgical aspirator or radiofrequency dissecting sealer) have been proven equal (but partly requiring complex equipment) in terms of blood loss as the most important parameter for patient outcomes.[13] In addition to primary haemostasis
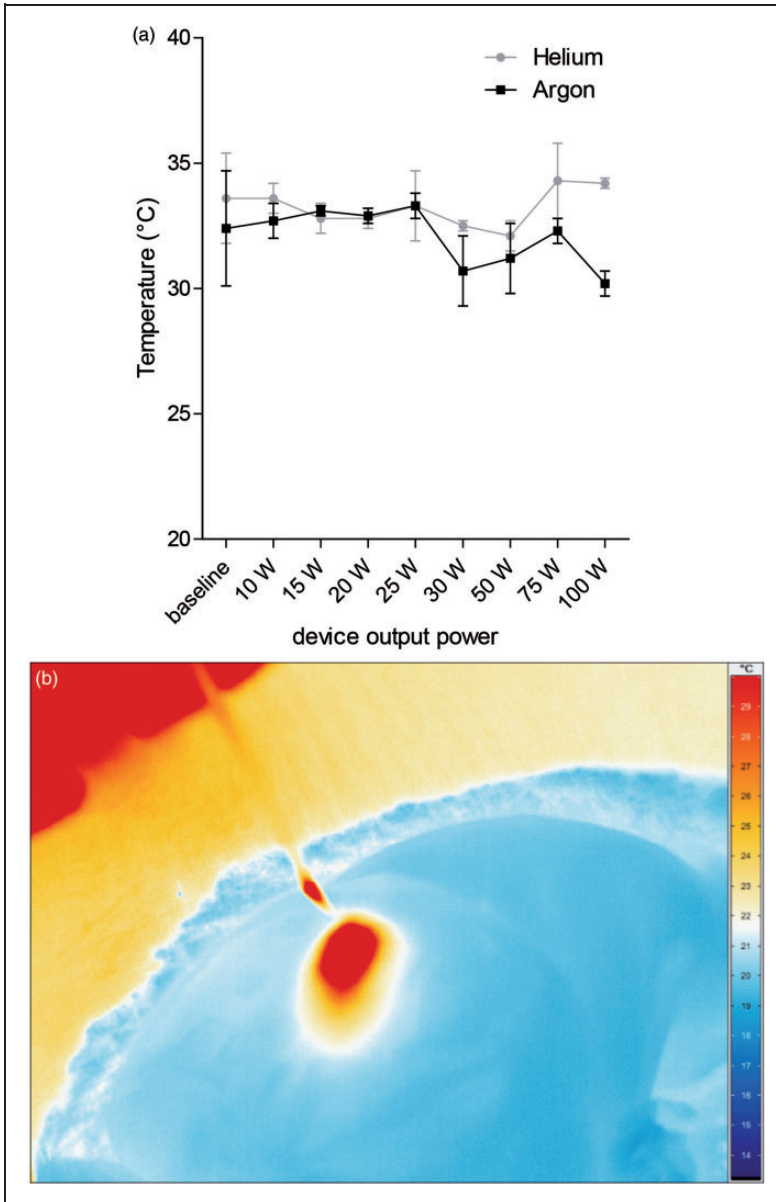
Figure 3. (a) Temperature at the liver surface before and after argon and helium plasma coagulation as measured with the infrared thermometer. Data are shown as mean ± standard deviation. (b) Helium plasma coagulation recorded with the thermographic camera at 100 W (typical results are shown).

during resection, many tertiary centres use techniques to seal the cut surface of the liver to achieve secondary haemostasis and prevent haemorrhage at a later stage.

The standard technique with which to achieve secondary haemostasis is APC.[14,30] Despite its widespread clinical use during the past three decades, only a few in-vivo

Table 1. Selected clinical chemistry, haematology, and blood gas analysis parameters.

Parameter	APC (n = 6)		HPC (n = 5)		P
	Pre	Post	Pre	Post	
Potassium [mmol/L]	4.40 ± 0.45	4.32 ± 0.35	4.28 ± 0.29	4.60 ± 1.00	n.s.
Creatinine [mg/dL]	1.17 ± 0.16	1.14 ± 0.15	1.23 ± 0.09	1.12 ± 0.10	n.s.
ALT [U/L]	37 ± 10	27 ± 9	50 ± 13	35 ± 9	n.s.
AST [U/L]	48 ± 13	54 ± 12	52 ± 16	50 ± 7	n.s.
INR	1.0	1.0	1.0	1.1	n.s.
APTT [s]	13 ± 0	14 ± 1	13 ± 1	14 ± 1	n.s.
WBC [g/L]	13.76 ± 5.57	11.14 ± 5.60	13.96 ± 2.03	11.97 ± 2.13	n.s.
Hb [g/dL]	10.30 ± 0.90	9.90 ± 1.20	10.90 ± 1.10	10.20 ± 1.20	n.s.
pH	7.5	7.4	7.4	7.4	n.s.
Lactate [mmol/L]	0.90 ± 0.30	0.70 ± 0.20	1.00 ± 0.30	0.90 ± 0.20	n.s.

Data are presented as mean or mean ± standard deviation. A P-value of < 0.05 is considered statistically significant. APC = argon plasma coagulation, HPC = helium plasma coagulation, ALT = alanine aminotransferase, AST = aspartate aminotransferase, INR = international normalised ratio, APTT = activated partial thromboplastin time, WBC = white blood cells, Hb = haemoglobin, n.s. = not significant.
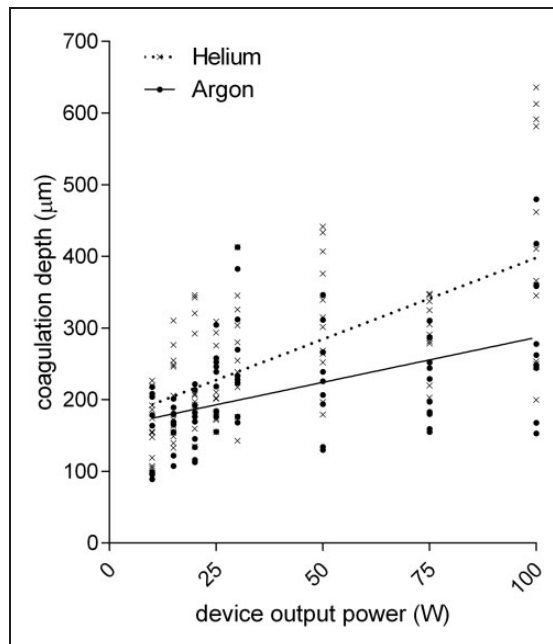

Figure 4. Coagulation depth following argon and helium plasma coagulation. Data are expressed as single values and linear regression.
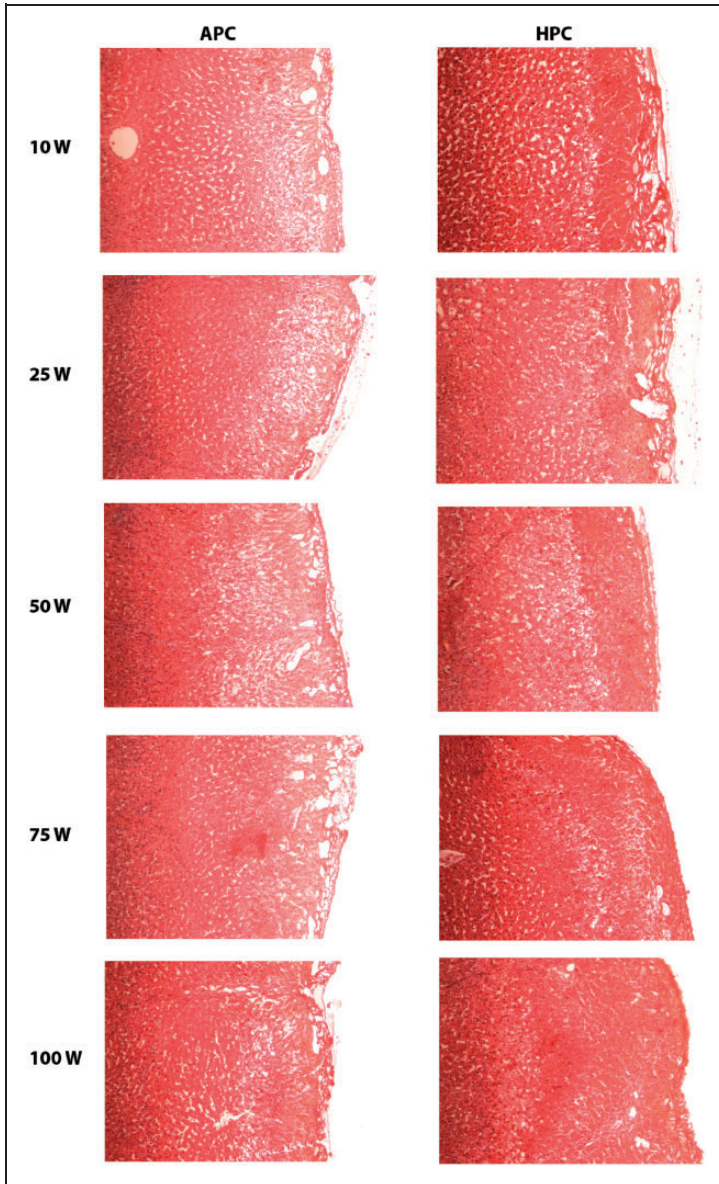
Figure 5. Histological samples following argon and helium plasma coagulation at different power levels of the coagulator device. Haematoxylin–eosin stain; magnification ×40. The coagulation depth can be determined by means of sharp distinction between the zone of necrosis at the liver surface and the vital liver tissue. APC, argon plasma coagulation; HPC, helium plasma coagulation.

studies have examined the effects of plasma coagulation on liver tissue. The present study was performed to determine the local tissue effects and systemic changes following plasma coagulation on porcine liver tissue with argon and helium gas. The CPC-1000 generator that was used in this study can be operated with both gases, allowing the side
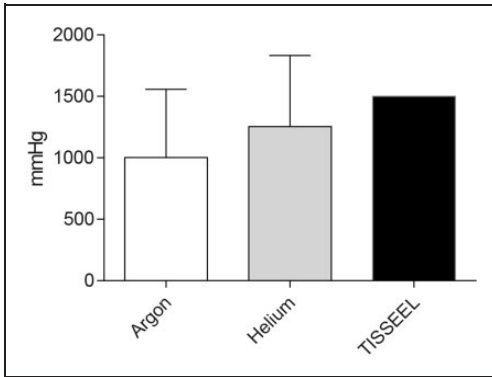
Figure 6. Burst pressure measurements on the liver cut surface following argon plasma coagulation, helium plasma coagulation, and fibrin sealing. Data are shown as mean ± standard deviation.

effects of different coagulator devices and techniques to be excluded. Another important advantage of the CPC-1000 generator in contrast to other plasma coagulation devices is the missing neutral electrode: the radio-frequency currency is returned as a capacitive displacement current from the patient surface to the grounded terminal of the plasma generator, requiring no neutral electrode. Therefore, the danger of electrical damage to tissue distant to the coagulation site is drastically reduced. Generally, comparison of existing studies is difficult because the factors influencing the coagulation effect (duration of activation, power setting, and probe distance) are only seldom standardised between the studies; furthermore, the carrier gas and coagulation devices differ among the studies.[15,16,18,19,30–33] This might be a reason why the reported coagulation depth differs between the studies: up to 4 mm on porcine skin,[1] 5 to 6 mm in human gastrointestinal tumours,[7] 0.75 to 1 mm in rat brain tissue,[33] and 0.6 to 0.68 mm in the uterus, ovary, and fallopian tube.[19] Besides the above-mentioned differences, the perfusion, water content, and connective tissue content of different organs have limited comparability. A study

examining HPC in an isolated perfused porcine liver model produced tissue damage of 0.25 mm at 40 W,[31] which is within the range we observed at 50 W (APC, $225 \pm 70 \, \mu m$; HPC, $315 \pm 87 \, \mu m$). We are the first to use the O2C device to measure the microcirculation following plasma coagulation. Sufficient superficial haemostasis was observed with both APC and HPC, beginning with low power settings. This impression was confirmed by the microcirculatory parameters and already occurs at 10 W. In this study, we standardised the probe distance and application time, and the same coagulation device was used; only the power settings and carrier gas varied. The depth of the coagulation zone could be precisely controlled through selection of the device output power level, while the slope of the power setting/coagulation depth curve was less steep for APC than for HPC. A coagulation depth of $144 \pm 55 \, \mu m$ (APC) and $157 \pm 45 \, \mu m$ (HPC) was achieved at the lowest setting of 10 W. Interestingly, the coagulation depth at the maximum power level of 100 W was deeper for HPC ($413 \pm 161 \, \mu m$) than for APC ($297 \pm 105 \, \mu m$). This appears controversial because helium provides a lower temperature in the plasma beam; however, it can be explained through the above-mentioned mode of action of plasma coagulation. At a higher temperature, carbonisation occurs and the electrical resistance distinctly increases, directing the plasma beam to other areas that are not yet desiccated and thus have lower electrical resistance. Thus, with a higher temperature, a less deep tissue effect can be achieved as with a lower temperature at the probe, where desiccation and increased electrical resistance occur later in the coagulation process. The difference in the achieved coagulation depth between helium and argon coagulation was marginal in the present study. Additionally, no difference was observed in the vessel-sealing effect between the two gases. The vessel-sealing effects of

APC and HPC were comparable with that obtained by the commercially available fibrin sealant, which seems appropriate for most clinical situations. No major differences between APC and HPC were observed. The significantly higher burst pressure in the ex-vivo measurements than in the perfused organs[25] can be explained by the missing resistance of the surrounding perfused blood vessels. Despite the electro-thermal coagulation effect, no temperature change could be measured immediately after coagulation (while the temperature during coagulation was lower for HPC). The rise in temperature needed for the coagulation effect is momentary; the temperature soon cools to the normal body temperature because of the very high blood flow within the liver. Contributing factors include the small coagulation area and the excellent perfusion of the liver. This phenomenon is also observed in radiofrequency ablation of liver lesions, in which the ablation effect is lost in close proximity to vessels.[34] The restriction of the coagulation effect in the present study can also be explained by the fact that no systemic changes in the clinical chemistry, haematology, or blood gas parameters were recorded. We found no major difference in the use of argon or helium for superficial liver coagulation in our experimental setting. The coagulation depth can be precisely controlled with the power setting of the coagulator device. The overall depth seems appropriate for superficial haemostasis of liver resection margins without harming deeper tissue; it might even be possible to coagulate the tissue close to the hilar structures. In a previous study, plasma coagulation of porcine small bowel was safe using low and medium power settings.[35] An advantage of plasma coagulation that was not addressed in the present study might be less tissue vaporisation, which is reportedly beneficial in terms of less smoke production in viral skin lesions.[1] Surgical smoke is an important issue in surgical research because of the potential risk of transmission of viral hepatitis during liver surgery.[36,37] However, whether plasma coagulation is superior to electrocautery in terms of this characteristic requires further examination.

Conclusion

We observed no significant differences in the use of APC and HPC on porcine liver tissue in an experimental model. Both techniques are equally safe and feasible for achievement of superficial haemostasis in liver tissue. This study can help to estimate the coagulation depth at different power settings for both carrier gases.

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