Mini-reviews

Increasingly, technology plays an important role in urology, and with this greater use comes the expected increase in regulation. Authors from the UK present a review of the physical properties of ablative technologies, evaluating efficacy and safety, and summarising guidance issued by the National Institute of Health and Clinical Excellence (NICE) where available. There are also reviews from the UK on haematuria, and on the pathology of bladder cancer from an international group of European authors.

Hot and cold technologies for tissue ablation in urology

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INTRODUCTION

In the UK, guidance on the safety and efficacy of interventional procedures is produced by the Interventional Procedures Programme within the National Institute of Health and Clinical Excellence (NICE) [1]. New minimally invasive procedures in urological surgery often involve the use of ablative techniques using various energy sources, with the possibility of different safety and efficacy profiles. In this review, we describe the physical properties of ablative technologies used in urological surgery, to inform any evaluation of the safety and efficacy of a procedure. Where applicable, guidance issued by NICE on the safety and efficacy of urological procedures using ablative techniques is summarized.

THERMAL ABLATION

Irreversible cell injury occurs when cells are heated to 46°C for 60 min [2]. With increasing temperature, the time necessary to induce cell death is shortened and at 60–100°C cell death is immediate and irreversible. Coagulation necrosis results in irreversible thermal damage to cells. Temperatures of >105°C result in tissue boiling, vaporization and carbonization; carbonization can retard optimal ablation [3]. These effects are summarized in Table 1 [4].

Electromagnetic energy can be used to thermally ablate (coagulate), in the form of radiowaves (radiofrequency, RF), microwaves and light (laser). The production of heat is also the basis for an alternative means of thermal ablation, high-intensity focused ultrasound (HIFU). The success of the thermal ablation depends on the energy source, applicators and tissue characteristics. Heat deposition is greatest around the electrode/probe, with less heat deposited in deeper tissues due to the rapid decline in energy density away from the electrode, as well as the resistance (impedance) to heat conduction within the tissue.

Many different minimally invasive thermal ablative techniques are described for treating benign and malignant tumours. The principal mechanism of tissue destruction is the same and does not depend on the frequency of the electromagnetic energy, i.e. whether radiowaves, microwaves or visible light, but the frequency determines the extent of the uptake and dissipation in the tissue. The heat generated (joules) is a product of the power applied (watts) and duration of application (seconds).

All thermal effects are influenced negatively by blood flow, by removing heat before the

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tumour is completely ablated (the heat-sink effect); this effect protects blood vessels and prevents bleeding of large vessels, and is a reason for incomplete ablation.

METHODS OF THERMAL ABLATION

ELECTROSURGERY

This broad term encompasses several different electrical methods used to heat and destroy tissue, and includes surgical diathermy, RF ablation (RFA), 'coblation' and microwave ablation. It does not include electrocautery or the use of electrically heated probes where the electricity does not pass through the body tissues.

Electrosurgery can be monopolar or bipolar. Monopolar devices use a single 'active' electrode applied to the target tissue; current is then dispersed to a grounding pad placed on the patient's skin at a remote location. Bipolar devices have two active electrode applicators, which are usually placed close together, to achieve contiguous ablation between the electrodes (e.g. forceps). The current passes only through the tissue in the forceps and not through the patient's body. For this reason bipolar circuits are generally safer than monopolar circuits.

Radiofrequency ablation

RFA is a temperature-controlled, and in some cases resistance-controlled, form of diathermy. A RF generator provides a RF alternating voltage on electrode(s) placed within the tissue. The resulting high-frequency alternating current (3.5–5 MHz) induces temperature changes in the tissue. The energy, as heat, dissipates rapidly with increasing distance from the electrodes, so that the highest temperature is always at the point nearest to the electrodes. For complete and adequate tissue destruction the entire tissue or tumour needs to be subjected to cytotoxic temperatures. The size and shape of the coagulated area depends on the probe type, length of exposed tip, and intensity of application, impedance and the duration of treatment. Multiprobe applicators, also referred to as tines, umbrella electrodes, multi-tined electrodes, multiple hooked electrodes, Christmas-tree electrodes or arrays, have been developed to increase the volume of coagulative necrosis. A limitation to RF energy deposition is the overheating that surrounds the active electrode; this can lead to local tissue charring, rising impedance and interruption of the RF circuit. To limit these effects, internally cooled devices have been developed, with saline solution or water contained around the electrode but not in direct contact with tissue.

TABLE 1 The temperature and tissue effects of ablation. Adapted from Odell [4]

	Effect		
Temperature, °C	Visible	Delayed	Mechanism
34–44	None	Oedema	Vasodilatation and inflammation
44–50	None	Necrosis	Disruption of cell metabolism
50–50	Blanching	Sloughing	Collagen denaturation
80–100	Shrinkage	Sloughing	Desiccation
100–200	Steam 'popping'	Ulceration	Vaporization
>200	Carbonization cratering	Larger ulcer	Combustion of tissue, hydrocarbons

Coblation

This technique uses a bipolar probe to generate a RF electric current applied to a conductive medium (usually saline), causing a highly focused plasma field to form around the energized electrodes to dissect and coagulate tissue. The plasma field dissects tissue, while a coexisting low-power current coagulates vessels. Coblation operates at lower temperatures than diathermy, with the potential advantage over diathermy of reduced damage to surrounding tissue with reduced postoperative pain and earlier healing.

Microwave

With microwave ablation, also known as microwave coagulation or thermotherapy, alternating ultrahigh-frequency (2450 MHz) waves emitted from a probe induce the rotation of water molecules and heat is produced. Microwave ablation therapy creates a predictable and reproducible area of tissue ablation. It appears to produce a haemostatic effect on surrounding tissues, theoretically reducing the risk of haemorrhage after the procedure. Microwave coagulation therapy has the advantage of other thermal ablative techniques in that ablation is rapid and the area of ablation is immediately hypo-echoic on real-time ultrasonographic monitoring, and therefore completeness of ablation can be easily monitored.

UROLOGICAL APPLICATIONS OF ELECTROSURGERY

Diathermy is widely used during tissue dissection and haemostasis in open and laparoscopic surgery, but not usually directly for tissue ablation. TURP remains the most common procedure for the surgical management of benign prostatic obstruction (BPO); diathermy is used (in cutting mode) to cut the enlarged gland into pieces small enough to be evacuated endoscopically. Traditionally this has been done using a monopolar electrode loop. More recently a bipolar loop was introduced, with the advantage of less bleeding and of being able to use saline for irrigation rather than electrically non-conducting liquids which can be absorbed, resulting in haemodilution ('TUR syndrome'). Endoscopic diathermy dissection is also the basis for transurethral incision of the prostate (TUIP), which is advocated in men with smaller prostates. TUIP is considered to be quicker, technically easier and with a lower incidence of retrograde ejaculation than TURP for men with prostates of <30 g.

Minimally invasive alternative therapies for BPO, using electrosurgery, are transurethral needle ablation of the prostate (TUNA), transurethral RFA prostatectomy (TURAPY), and transurethral electrovaporization of the prostate (TEVAP).

In TUNA, RF energy is delivered by needles inserted, under urethroscopic and thermosensory control, directly into the lateral lobes of the prostate to induce coagulative necrosis [5]. TURAPY is applied by a catheter consisting of a RF electrode introduced into the bladder and held in place by a retaining balloon, but is now rarely used [6]. In TEVAP, prostatic tissue is removed by vaporization and coagulative necrosis. The

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technique is similar to TURP, except for the electrode (Vaportrode®, ACMI Corp, Southborough, MA, USA) used to vaporize the obstructing tissue. The current density across the Vaportrode is not uniform, with the highest current density at the edges of the electrode, and the depth of the vaporization zone is 3– 4 mm, with a coagulation zone of 1–3 mm [7].

NICE has issued guidance on TUNA [8] and TEVAP [9]; for both procedures the current evidence on the safety and efficacy appears adequate to support their use, provided the normal arrangements are in place for consent, audit and clinical governance. The long-term efficacy has yet to be established.

Percutaneous RFA has applications for treating renal cancer when nephrectomy is contraindicated [10]. NICE has issued guidance on the use of percutaneous RFA for renal cancer [11]; 'Limited evidence suggests that percutaneous RFA brings about reduction in the tumour bulk and the procedure is adequately safe. However, the evidence of its effect on symptom control and survival is not yet adequate to support the use of this procedure without special arrangements for consent, and for audit or research'.

Coblation has been used for such diverse reasons as tonsillectomy, inferior turbinate reduction, and nucleoplasty for decompression of herniated vertebral discs, but does not appear to have been used in urological surgery.

Transurethral microwave thermotherapy (TUMT) has been used for many years to treat BPO and for painful perineal syndrome thought to be due to prostatic inflammation. Different theories were proposed for the mechanism of action, e.g. change in blood flow, damage to nerve endings or induction of apoptosis. The technology of TUMT has developed since its introduction in 1994. Tissue is ablated by heating the prostate via a urethral catheter to >46°C to induce coagulative necrosis [12]. Urinary retention is a relatively common after treatment, in the short-term, as the heating induces swelling (through oedema). TUMT has been refined to take account of the heat-sink effect, with the development of feedback microwave thermotherapy to control the treatment according to an individual's response to the microwaves [13]. The advantages of TUMT are that it can be applied as an outpatient procedure under local anaesthetic

ULTRASOUND

Sound waves are compression waves in air, which can also be transmitted by solid matter. Compression waves with a frequency over the limit of human hearing of 20 kHz are known as ultrasonic. Diagnostic ultrasound uses low-energy waves of a very high frequency (up to 10 MHz). Therapeutic ultrasound uses a lower frequency, but much higher energy (greater amplitude). Ultrasonic energy affects tissue through two different mechanisms, cavitation (akin to boiling) mainly in water-containing tissue, and internal friction resulting in tissue destruction; heat is produced.

HIFU, also known as ultrasound ablation, focused ultrasound surgery and pyrotherapy, relies on the same principles as conventional ultrasound. Sound waves, at higher amplitude than used in the diagnostic setting, delivered via an ultrasound transducer mounted in a water reservoir, and focused into a high-energy beam, results in the selective thermal ablation of the target tissue with no damage to adjacent tissues [14]. When HIFU is used for tumour ablation its optimal effect is in treating small tumours of 0.4–1 cm in diameter. Technological improvements might allow the treatment of larger tumours in the future. HIFU might activate platelet aggregation and adhesion, and this haemostatic effect might prevent bleeding complications after tumour ablation [15].

UROLOGICAL APPLICATIONS OF ULTRASOUND ABLATION

HIFU has been used to treat localized tumours of the prostate, kidney and bladder [16]. The extent of tissue ablation can be monitored either by real-time ultrasonography or MRI. There are limitations, e.g. an ablation of the whole prostate can take up to 6 h, as the machine resets its position repeatedly as it systematically treats the whole gland.

NICE has issued guidance on the safety and efficacy of HIFU for prostate cancer; it appears to be safe and effective, as measured by the reduction in prostate specific antigen levels, but the effects on health-related quality of life and long-term survival are uncertain [17].

PHOTOCOAGULATION

Laser light is coherent, collimated and monochromatic; the type of laser reflects the components of the solid, liquid or gas that constitutes its active medium and determines the wavelength of the radiation produced. Laser light can be described according to whether the beam is continuous, pulsed, or quality-switched. The mechanism of laser surgery can be to ablate, incise, vaporize, resect and dissect, depending on the laser's wavelength, power and type of emission (continuous or pulsed). The wide choice of laser variables and modes of delivery permit a close control of the desired effects. The laser energy can be delivered by direct contact, endoscopically or interstitially.

YAG lasers use yttrium-aluminium-garnet crystals as the lasing medium, and can be combined with neodymium, erbium or holmium. A Nd:YAG Laser emits a near infrared radiation at 1064 nm or 1320 nm, and has a penetration depth of 3–4 mm. It can be delivered in a long pulse or continuous wave to cut tissue or, because of its deep penetration, can be used to coagulate and vaporize tissue. When Nd:YAG laser light at 1064 nm is passed through a potassium-titanyl-phosphate (KTP) crystal the wavelength is halved to 532 nm, and the emitted green light in continuous wave mode can incise and vaporize tissue. The Ho-YAG laser emits a mid-infrared beam at 2070 nm with good incisional and haemostatic properties.

Diode lasers have an operating wavelength of 600–1600 nm and are absorbed relatively independently of tissue type. The diode laser compares favourably with several of the other thermal lasers; it results in a slightly higher degree of absorption by tissue than does the Nd:YAG laser.

Interstitial laser photocoagulation, also referred to as interstitial laser therapy, interstitial laser coagulation, laser-induced interstitial thermal therapy, is a process whereby laser light can be delivered into lesions in solid organs, endoscopically or percutaneously under image guidance via a thin optical fibre.

UROLOGICAL APPLICATIONS OF LASER PHOTOCOAGULATION

The ablation of tissue by laser light has many applications in urology, particularly for

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treating BPO. These include interstitial laser coagulation using the Nd:YAG or diode laser, which is applied directly into the prostatic tissue, KTP laser vaporization and holmium laser prostatectomy. NICE has issued guidance on KTP laser vaporization [18] and holmium laser prostatectomy [19] for the management of BPO. Both procedures appear to be adequately safe and effective; there were insufficient data to assess the long-term efficacy of KTP laser vaporization.

COLD ABLATION

CRYOABLATION

Cryoablation is the use of low temperatures to destroy tissue; the freezing of tissue to −40 to −80°C, and subsequent rapid thawing, leads to disruption of cell membranes and induces cell death. Argon gas or liquid nitrogen is used to achieve such cooling.

UROLOGICAL APPLICATIONS OF CRYOABLATION

Cryosurgery has been used for many years to treat prostate cancer and renal tumours, and is currently undergoing a revival of interest. Cryoablation has traditionally been applied urethrally; more recently, alternative techniques using cryoprobes inserted through small skin perineal incisions, under image guidance, have been applied for treating prostatic tumours. Damage to adjacent tissues, fever, pain and haemorrhage are the commonly cited potential adverse events of cryoablation.

NICE has issued guidance on the safety and efficacy of cryotherapy for recurrent prostate cancer. Cryotherapy appears to be safe and effective as measured by the reduction in PSA levels, but the effects on health-related quality of life and long-term survival are uncertain [20].

CONCLUSION

We describe various methods by which tissue can be heated (or cooled) to remove obstructing tissue. There is constant innovation in the technologies used, although the principles of tissue ablation remain the same. When choosing a technology, the clinician will be mindful of the aims of the intervention and the possible adverse events that might result from its use. New technologies aim to be at least as effective as existing techniques but with lower morbidity. The clinical and cost-effectiveness of alternative minimally invasive interventional procedures needs to be defined.

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CONFLICT OF INTEREST

None declared.

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Abbreviations: **NICE**, National Institute for Health and Clinical Excellence; **RF(A)**, radiofrequency (ablation); **HIFU**, high-intensity focused ultrasound; **BPO**, benign prostatic obstruction; **TUIP**, transurethral incision of the prostate; **TUNA**, transurethral needle ablation of the prostate; **TURP**, transurethral resection of the prostate; **TURAPY**, transurethral RFA prostatectomy; **TEVAP**, transurethral electrovaporization of the prostate; **TUMT**, transurethral microwave thermotherapy; **KTP**, potassium-titanyl-phosphate.

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