Image guided cryoablation of renal cell carcinoma: The Leeds experience

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History of cryoablation
From 2500 BC, the ancient Greeks used cold temperature to treat ailments in order to decrease inflammation and relieve pain, e.g. they described sitting patients in cold streams to alleviate pain. The true concept of cryotherapy was only realised in the 18th century, when English doctor Dr James Arnott (1797-1883) was the first to use cold temperature to destroy tissue with a combination of ice and salt. As this could only be applied topically, he had managed to treat superficial tumours such as breast and cervical tumours.¹

In the 1980s, based on the principle for air conditioning and refrigeration where atmospheric air warms when compressed and cools during expansion, liquid air and carbon dioxide (CO₂) were utilised as cryogens. They were used clinically to treat various skin conditions such as skin cancer.²

In the 1990s, liquid nitrogen was recognised for its importance as a cryogen in surgical application and expanded the clinical indications into treating oral cancers, ophthalmologic and gynaecologic conditions.³ In 1963, Irving Cooper, a neurosurgeon from New York, reported the use of a liquid nitrogen cryoprobe that could achieve a temperature of -196°C and used this to treat inoperable brain tumours and Parkinson’s disease.⁴

The availability of the cooled cryoprobe with liquid nitrogen had revolutionised cryoablation treatment, where the probe could be placed into the deeper organ for treatment. However, the limitation was the inability to monitor the ice ball margin and this caused significant complications when treating deeper organs such as prostate glands resulting in urethral injury.⁵

In the 1980s, the development of image guided treatment using intra-operative ultrasound guidance to treat liver tumour sparked a renewed interest in image guided cryoablation.⁶

In the 1990s, a new cryoablation technology was discovered using the Joule-Thomson principle and the introduction of the argon gas system. This system involves driving high pressure argon gas through smaller needles (as small as 17-gauge). The development of the ultrathin needle has allowed a minimally invasive approach and this needle can be passed through the skin with a laparoscopic approach or under imaging guidance.⁷⁻⁸

Mechanism of cell death by cryoablation
There are three important processes:⁹⁻¹⁴
1. Intracellular ice crystal formation – occurs with rapid freezing or freezing to extreme low temperature. This causes direct injury to the cellular content or the cellular membrane
2. Extracellular ice crystal formation – occurs with slower freezing. The injury is caused by the osmotic gradient causing fluid shift from intracellular space into the extracellular space, leading to cellular dehydration and death.
3. Local tissue ischaemia due to micro vessel thrombosis.

Epidemiology of renal cell carcinoma (RCC)
The incidence of kidney cancer is rising worldwide. There are more than 7,500 new cases a year in the UK.¹⁵ This has been partly due to the increase of incidentally detected RCC from wider use of radiological imaging¹⁶ and it is also related to increased incidence of renal cancer in the general population. Cigarette smoking and obesity are the two most important causal and preventable risk factors, accounting for 20% and 30% of RCC respectively.¹⁷,¹⁸

What would be the ideal therapy to treat these smaller renal cancers? Ideally, the technique should preserve the kidney, avoid the need for open surgery and be performed as a day case procedure. One advantage of cryotherapy when compared to the heat-based energy is the ability to visualise the ice ball on imaging. This allows accurate assessment of the treatment margin so as to avoid damaging the surrounding tissue.

CT guided cryoablation: The Leeds approach
Our percutaneous renal radiofrequency ablation (RFA) programme was established in 2004 at our institution, initially offering RFA of RCC and we started offering cryoablation from 2008. All the patients were referred through our local urology multidisciplinary team (MDT) meeting. The inclusion criteria for consideration of renal ablative treatment are: non-surgical candidate with small incident renal tumour, renal tumour in solitary kidney, synchronous primary renal tumour, patients with Von-Hippel-Lindau (VHL) disease or impaired renal function. In addition, depending on the clinical situation, patient’s choice and metastatic RCC undergoing immunotherapy were also considered.

Following MDT, the patients were then seen in the outpatient consultation clinic by both the consultant urologist and radiologist. All patients were referred to the hospital pre-assessment clinic to assess their fitness for general anaesthesia and screen for day case admission. Routine baseline laboratory investigations were performed such as clotting screen (INR < 1.5 was required at the time of treatment), renal function test (creatinine measurement) and full blood counts.

Biopsy procedure
All patients undergo biopsies at the time of ablation of the renal tumour as part of their standard clinical care in our institution. A co-access sheath is usually inserted into the renal tumour under CT guidance. All biopsies were performed with a co-access sheath (Boston Scientific, MA, USA) system using a 16-gauge outer sheath and an 18-gauge core biopsy needle gun (Boston Scientific, MA, USA).

Cryoablation treatment
All procedures are performed under general anaesthesia as a preferred option by the anaesthetist. All patients received broad spectrum antibiotics (co-amoxiclav 1.2g) 12-hourly on the day of treatment and a 10-day course of oral ciprofloxacin (500mg twice daily), routinely administered prophylactically for all renal ablation patients.¹⁹ The treatment is performed as an elective procedure in all patients with routine admission the day before or on the day of treatment if they are fit and observation overnight post-proce-
dure. All patients had dynamic contrast enhanced (DCE) cross sectional (CT or MRI) imaging before and after cryo. In our institution, we routinely performed DCE-MRI at baseline, 1, 3 and 6 months post cryo and annual CT for full staging including chest and kidneys for a period of 10 years as part of our Yorkshire Cancer Network (YNCN) protocol.

All renal cryoablation treatments are performed in the CT interventional suite by the consultant radiologist using the cryo generator system (Seed Net, Galil Medical, MN) and a range of cryoprobes such as Ice Seed, Ice Sphere and Ice Rod (Galil Medical, Israel). The patient usually lies in the lateral or prone position for treatment. All the needle cryoprobes are inserted under CT guidance and the number of cryoprobes required depends on the size and geometry of the renal tumours. The ice ball can be seen during treatment and this allows accurate estimation of the treatment margin. Multi-planar reformating is useful during treatment, this allows assessment of the sculptured ice ball to ensure it completely engulfs the whole renal tumour (figures 1A and 1B).

**Pneumo-dissection technique**

This is used when the renal tumors lie in close proximity (<1cm) of the bowel loops or surrounding vital organ during treatment. This could be due to the location of the tumour (anterior and midpolar location) or lack of intra-abdominal fat. We routinely performed this with a 16G sheathed needle (Boston Scientific, MA, USA) and usually 150 to 500mls of sterile air or CO₂ is instilled to displace the structure from the treatment margin (figure 2).

**Warm pyeloperfusion technique**

Retrograde pyeloperfusion with warmed saline/dextrose should be considered when treating centrally located renal tumour. Nowadays, all pyeloperfusions are performed by a urologist in our CT interventional suite. A CT scout view is performed to confirm the end flushing catheter position and, if in doubt, some contrast may be injected, a repeat scout film can be performed to ensure the position is correct. The ice ball treatment margin can be clearly visualised during treatment and minimise the injury to the ureter (figure 3).

**The Leeds Experience to date**

In Leeds, from May 2008 to May 2012, 60 patients (37 male and 23 female) with 65 renal tumours were treated with percutaneous cryoablation. The age range was 22-86 years (mean=68) and the mean tumour size 2.5cm.

Of the 65 treated renal tumours, 64 were completely ablated (61 in a single session, two after a second session and one after a third session) with a follow-up period ranging from 1-48 months. One patient declined re-treatment. This gives an overall technical success rate of 98.4%.

There were three complications treated conservatively, including self-limiting subcapsular haematoma (n=1), retroperitoneal haematoma (n=1) and transient lumbar plexus injury (n=1). There was one predicted ureteric injury from treating a centrally located tumour adjacent to the renal pelvis, requiring long-term ureteric stenting.

**Conclusion**

Percutaneous image guided cryoablation is a safe, effective and minimally invasive treatment for small RCC. There is a definite learning curve for cryo-needle placement and the rate of residual disease would improve with operator’s experience. Both pneumodissection and warm pyeloperfusion should be considered for treating tumours close to the vital organs and collecting system/ureter.

**References**