Closed argon-based cryoablation of bone tumours

We report our experience with a new technique for cryosurgical ablation of bone tumours which allows accurate determination of the temperature and freezing time within a cavity of any geometrical shape.

Between 1997 and 2000, 58 patients diagnosed with 13 malignant and 45 aggressive benign bone tumours underwent argon-based cryoablation. This technique includes removal of the tumour by curettage and filling the cavity with a gel medium into which metal probes are inserted. Argon gas is delivered through the metal probes and both time and temperature are computer-controlled. After formal reconstruction, all patients were followed for more than two years. None had skin necrosis, infection, neurapraxia or thromboembolic complication. Fractures occurred in two patients (3.4%) and the tumour recurred in two patients (3.4%).

Since its introduction in the early 1970’s, cryosurgery has been used as an adjuvant to curettage in the management of a variety of bone tumours.1-16 This technique entails curettage and burr-drilling of the tumour cavity, instillation of liquid nitrogen (LN) and reconstruction of the cavity using implants and polymethylmethacrylate (PMMA).5,15,17 Cryosurgery has achieved good local control of aggressive benign, malignant, and metastatic bone tumours.1-16 Defined as an intralesional procedure, it has the advantage of preserving adjacent joints.5,7 The application of LN directly into the cavity has several drawbacks: first, there is no control of the overall freezing time or of the temperature at different sites within the cavity; secondly, it is a gravity-dependent procedure and thus the liquid cannot reach areas of the tumour cavity which are situated above the fluid level.

Between 1997 and 2000, we treated 58 patients with aggressive benign and malignant bone tumours using a novel technique. The tumour cavity is emptied and then filled with a gel medium into which cannulated metal probes are inserted. Freezing argon gas is then injected through the metal probes by a computer-controlled delivery system. The surrounding gel acts as a conducting medium, distributing the freezing temperature equally throughout the cavity. The periods of time and depth of temperature in all areas of the cavity are measured and controlled by computers. The use of a viscous gel enables any shape of tumour cavity to be filled, regardless of gravity.

There was no case selection during the study period; all patients who met the criteria for cryosurgical ablation were treated in the same way. All patients in the current study were subsequently followed for more than two years (37 to 69 months; median, 49 months). We present the surgical concept and technique of argon-based closed cryoablation, together with all related complications and the rate of local tumour control.

Patients and Methods
Between 1997 and 2000, 58 patients with bone tumours were treated. There were 37 men and 21 women, ranging in age from 8 to 80 years (median, 25 years). Follow-up ranged from 37 to 69 months (median, 49 months). Diagnoses included 13 primary malignant and 45 benign aggressive bone tumours (Tables I and II). All nine patients with chondrosarcoma had a low-grade lesion and the two patients with Ewing’s sarcoma had tumours which were confined to the medullary cavity of the affected bone. Before surgery, all patients underwent staging studies which included plain radiography, computed tomography (CT), magnetic resonance imaging (MRI) of the affected site, and bone scintigraphy. At the conclusion of the staging studies, core needle biopsy was obtained under CT guidance in every patient.
Operative technique. The basic steps of cryosurgery include: 1) wide exposure of the affected bone, mobilisation of fasciocutaneous flaps and the neurovascular bundle and opening of a cortical window, 2) removal of the tumour by curettage and high-speed burr drilling, 3) intralesional freezing and 4) mechanical reconstruction.\textsuperscript{5,17}

After exposure of the affected bone and mobilisation of the surrounding soft tissues, a cortical window the size of the greatest longitudinal dimension of the tumour is made. The tumour is approached through the retained, thinned or destroyed cortex to minimise bone loss. All tumour bulk is removed with curettes. This is followed by high-speed burr drilling through the inner reactive shell using the Black Max (Anspach, Lake Park, Florida). Fasciocutaneous flaps, surrounding muscles, and neurovascular bundles are protected by shielding with Gelfoam (Upjohn, Kalamazoo, Michigan).
The CRYO-HIT system (Galil Medical, Yokneam, Israel) is used for cryoablation. It has a work station which includes a monitor, control panel and housing unit for six gas cylinders, five of which contain freezing gas (argon) and the sixth, thawing gas (helium) and connecting cables and metal probes of differing sizes to accommodate different volumes of tumour cavity (Fig. 1). It is a closed system delivering argon gas through a metal probe so as not to be in contact with the ablated tissue, and having a default temperature of -190°C. Using the same probes and delivery system, helium gas with a default temperature of 35°C is introduced to produce immediate thawing. The temperature at the tip of each probe is measured separately.

Trial positioning of the probes within the tumour cavity is carried out, taking care to select the largest possible sizes and to distribute the probes widely within the cavity. Between one and three probes are used according to the volume of the cavity (Fig. 2). The probes are then removed and the cavity filled with a viscous surgical gel (Surgilube; Fougera, Melville, New York). This product is a sterile, surgical lubricant, which is routinely used in the fields of urology and gynaecology. It is composed of chlorhexidine gluconate, a water-soluble, non-staining, and biologically inert substance. Care is taken to prevent spillage over the rim of the cavity. The probes are then repositioned within the gel, a thermocouple positioned along the inner wall of the tumour cavity, and cryoablation is performed. A controlled flow of argon gas is delivered through the probes while the temperature at the tips of the probes is continually monitored. The temperature falls rapidly and an ice ball composed of frozen gel grows in a centripetal fashion towards the walls of the tumour cavity until it fills the entire space (Fig. 3).

Cryoablation continues for five minutes from the point at which the temperature around the walls of the tumour cavity, as measured by the thermocouple, reaches -20°C or below. During cryoablation, the surrounding soft tissues are irrigated with saline solution to restrict the possibility of spillage and thermal injury. Thawing is then achieved by introducing warm helium gas through the same probes. The ice ball melts within two minutes. A single freeze-thaw cycle is performed. The probes are then removed, the tumour cavity is irrigated with saline to remove the remaining gel and reconstructed with an implant and polymethylmethacrylate. When this is undertaken near a weight-bearing area, autologous bone grafts are placed beneath the subchondral surface.

Routine peri-operative antibiotic therapy, with a second-generation cephalosporin, is administered for two weeks from the day of surgery, intravenously during the first two days and thereafter orally. The wounds are examined on the third day. If the skin is intact, passive and active movement of the adjacent joint is started. Patients with a lesion of the lower limb remain non-weight-bearing for six weeks. Radiographs are then performed to ensure that no fracture has occurred. If healing is progressing satisfactorily, partial
weight-bearing is allowed for four weeks and full weight-bearing thereafter.

Patients were seen in the outpatient clinic every three months and radiographs were taken at each visit. All clinical records and imaging studies were analysed by an orthopaedic oncologist (JB) and a musculoskeletal radiologist. Any wound complication, neurapraxia, fracture, local recurrence or joint changes were recorded.

**Results**

None of the patients had skin necrosis, infection, neuropraxia or thromboembolic complication. Post-operative fractures occurred in two patients (3.4%) during the first five months after surgery, following direct trauma in one patient and prohibited weight-bearing in the other. Both fractures occurred in the lower limb, one in the proximal femur and one in the proximal tibia. Both united with splintage and strict non-weight-bearing for a mean of four months (Fig. 4).

Local recurrence of tumour was observed in two patients (3.4%), after nine and 13 months. These patients had an aggressive benign lesion (giant cell tumour and aneurysmal bone cyst), both of which presented with extensive bone destruction and invasion of the soft-tissues. These recurrences occurred at the bone-PMMA interface and were treated with curettage and repeated cryoablation. More than two years after these procedures, there were no further signs of recurrence. No patient with a primary malignant tumour had a local recurrence. At the most recent follow-up, none of the study patients showed evidence of degenerative changes in an adjacent joint.

**Discussion**

Prior to this study of 58 patients we had extensive experience with the traditional method of cryosurgery, which entails pouring liquid nitrogen directly into the tumour cavity.\(^5,6,9,10\) We hypothesized that to use a controlled system to deliver the cryogenic substance and the use of a cold-conducting medium, would give a more efficient treatment.

The semi-liquid consistency of the gel used in this series allows complete filling of any cavity, in any anatomical site and against gravity. The gel functions as a cold-conducting medium, lowering the temperature evenly throughout the space. The use of a computerised delivery system allows accurate monitoring of the argon flow and enables careful control of the temperature at the tip of each probe. The determination of the overall freezing time in the current study is based on our hypothesis that five minutes of continuous freezing with the current method is equal in efficacy to two cycles of freezing with the traditional open technique of cryoablation, pouring liquid nitrogen for a period of one to two minutes.\(^5\)

The delivery of cryogenic fluid through metal probes has been previously reported. In 1985, Jacobs and Clemency\(^18\) reported their experience with 12 patients who underwent cryoablation of giant cell tumours of bone by means of malleable lead probes through which liquid nitrogen was delivered. The temperature within the tumour cavity was monitored with a thermocouple, and the flow of liquid nitrogen was turned off prior to reaching the desired freezing temperature.\(^7\) They speculated that this system, which prevents uncontrolled spillage of liquid nitrogen, would decrease the rate of post-operative fractures, but there were six fractures in five of their patients.\(^18\) Possible drawbacks of their technique, which might have been associated with a high rate of fracture include suboptimal control of liquid nitrogen flow resulting in a wide range of freezing times and temperatures within the cavity. This could have caused excessive freezing, and uncertain reconstruction of the cavities without the use of PMMA and implants.\(^18\) Argon-based systems have been shown to achieve a more rapid rate of freezing than liquid nitrogen-based systems\(^19,20\) and a more precise control of temperature and time.

Cold-related soft-tissue injuries (skin necrosis, infection, and neurapraxia) usually occur during the first few weeks after the procedure; fractures and local recurrences usually occur within the first two years.\(^3,4,9\) As all patients in this series were followed for more than five years, it is reasonable to assume that a longer follow-up would not significantly change the outcome. None of the 13 patients who

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**Fig. 4**

An anteroposterior radiograph of an undisplaced pathological fracture (arrow) of the femoral neck, six weeks after surgery. The patient had been walking with full weight-bearing on the operated extremity against explicit instructions not to. The fracture united clinically and radiologically after four months of non-weight-bearing.
had a primary malignant tumour of bone developed a local recurrence.

The current study focuses on the concept and surgical technique of argon-based and computer-controlled, closed cryoablation of bone tumours. The main advantages of this system are precise control of the freezing temperature and duration, and the use of a gel medium which evenly conducts the freezing temperature throughout the tumour cavity. This technique, which is simple to perform achieved good local tumour control with a low rate of complications.

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References