It may be that cytochrome P450 isoenzymes differ from each other in catalytic activity, substrate specificity, or inducibility by xenobiotics (9).

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First Clinical Experience with a Noninvasively Extendable Endoprosthesis: A Limb-Saving Procedure in Children Suffering from a Malignant Bone Tumor

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Abstract: A modular endoprosthetic system that can be extended noninvasively has been applied for the first time in a growing child who underwent a tumor resection in his leg. The main goal of the study was to test the extendable mechanism that noninvasively corrects leg length differences caused by growth disturbances of the affected leg. The use of this endoprosthetic system resulted in good restoration of function. Six extensions were performed resulting in 19.5 mm of prosthetic growth. Unfortunately, an ingrown toenail caused infection of the endoprosthesis, and the infection necessitated extirpation of the prosthesis 15 months postoperatively. Two months later the patient died of acute leukemia. Analysis of the endoprosthesis revealed some manufacturing shortcomings, none of which impaired the function of the endoprosthesis. **Key Words:** Osteosarcoma—Extendable endoprosthesis—Limb salvage—Modular—Tumor—Clinical study.

Malignant bone tumors are mainly encountered in the femur and knee area. Most cases of osteosarcoma occur in children and adolescents. Fortunately, in many cases it is possible to save the leg (1,2). Adjuvant chemotherapy, local resection of the involved bone and adjacent tissue, and replacement by an endoprosthesis provide the opportunity to realize a good cosmetic and functional result (3). For children, however, the other healthy leg grows in excess of the resected leg because resection of the knee region in children implies the loss of the distal femoral and proximal tibial epiphysis.

An endoprosthetic system that includes an element of adjustable length to match the growth of the other leg has been developed to allow growing children to benefit from the limb-saving procedure (4). Extension can be performed noninvasively, thus avoiding operations for adjustment. Consequently, the risk of infection is diminished. The system has a modular design to allow many different compositions with a limited number of modules.

The lengthening element (5) consists of 2 tubes. Extension is achieved using an electromagnet placed around the leg. It causes rotation of a small permanent magnet in the inner tube, and the magnet drives a motion screw via a gearbox. This screw rotates in

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the outer tube and forces the 2 telescopic tubes apart. Friction forces are limited by a polytetrafluorethylene (PTFE) layer covering the sliding parts (6). To shield the lengthening element from moisture, a bellows made of silicone rubber is glued to the lengthening element. After successful in vitro testing (5) and animal studies (7), the Medical Ethics Committee of the University Hospital Groningen approved a clinical trial with 3 patients. The first clinical trial is the subject of this paper.

Materials and methods

The endoprosthesis, composed from the Modular Endoprosthetic System, consisted of a lengthening

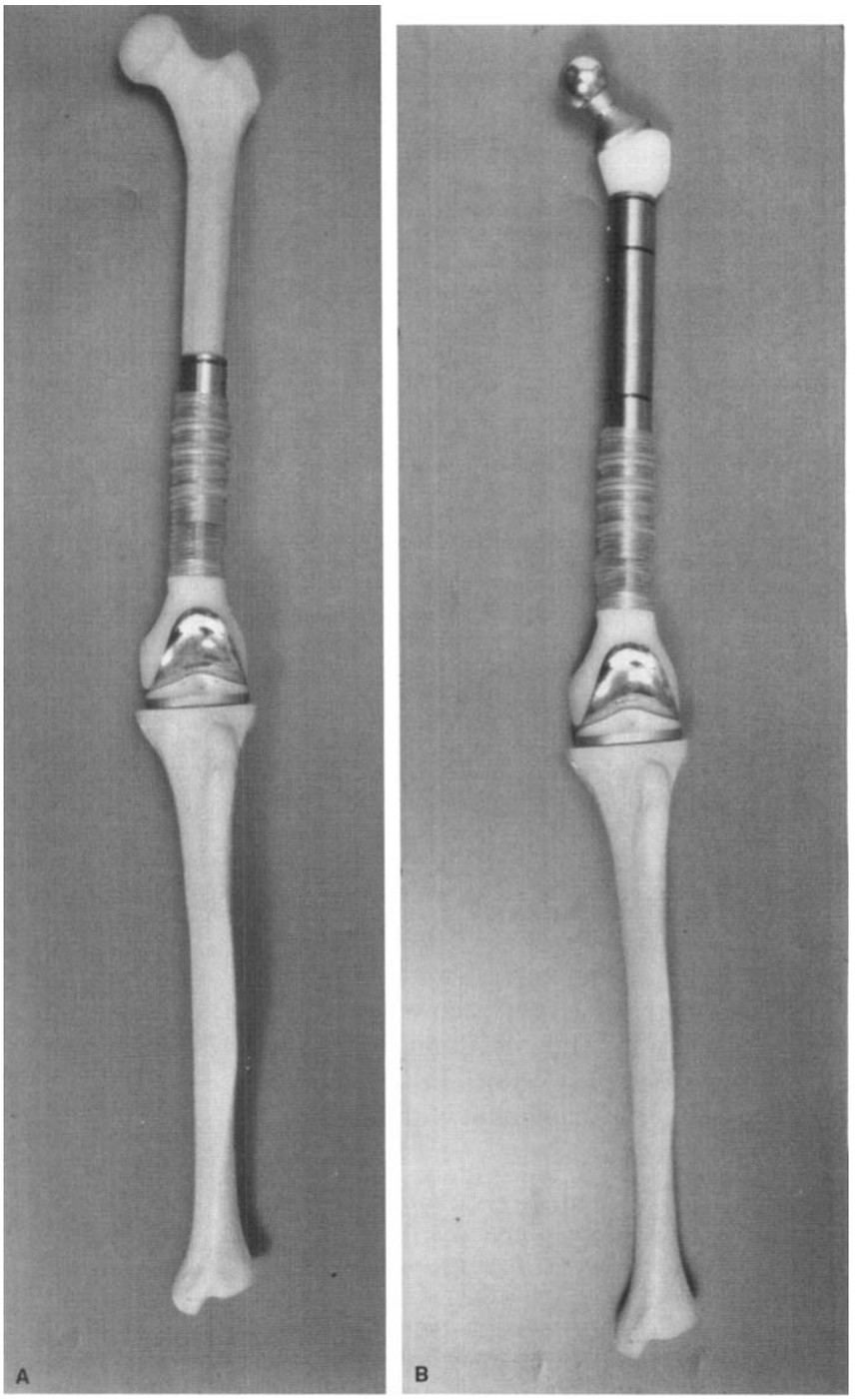

FIG. 1. The photographs show two configurations of the modular endoprosthetic system: an endoprosthesis to be used after distal femur resection **(A),** and an endoprosthesis to be used after total femur resection **(B).**

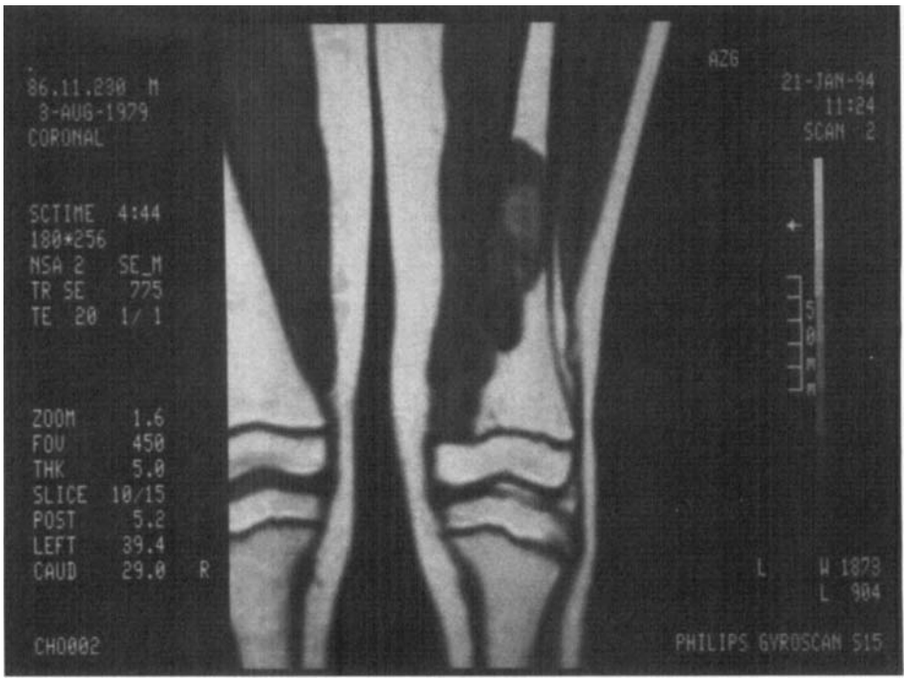

FIG. 2. Shown are the results of magnetic resonance imaging of the tumor showing soft tissue spread.

element, a left semiconstrained knee prosthesis, and a stem for femoral fixation (Fig. 3). Fixation to the remaining part of the tibia was performed by a stem cemented in the medullary canal. Attachment to the remaining part of the femur was realized with a custom-made, press-fit stem on which the contours of the bone were transposed. Extracortical side plates with unicortical screws provided for primary rotation stability. At the Groningen University Hospital such attachments had been applied successfully (1,3). The knee prosthesis, stems, and conical couplings were made by Waldemar Link, Hamburg, Germany, and the lengthening element by the Prototype Manufacturing Workshop, University of Twente, Enschede, Holland.

A 14-year-old boy had an osteosarcoma at the distal metaphysis of the femur. Magnetic resonance imaging (MRI) (Fig. 2) showed a wide tumor spread into the soft tissues. The patient was treated successfully by chemotherapy (cisplatin, doxorubicin, ifosfamide, and high dose methotrexate).

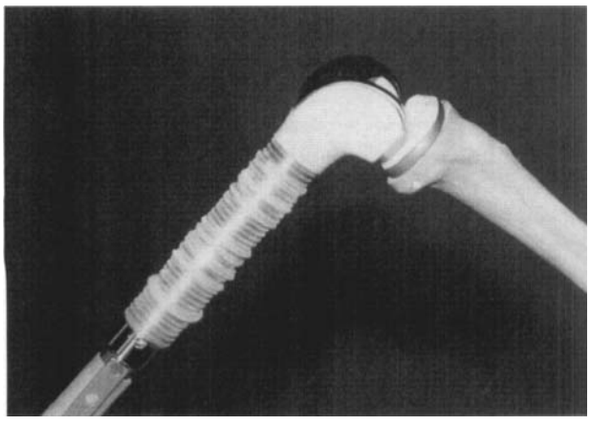

FIG. 3. The endoprosthesis used in the described case study is shown.

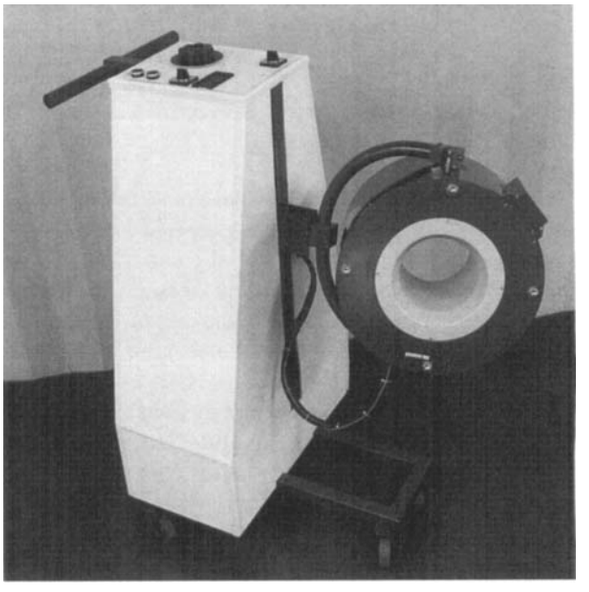

FIG. 4. Shown is an electromagnet on a trolly used to extend the endoprosthesis.

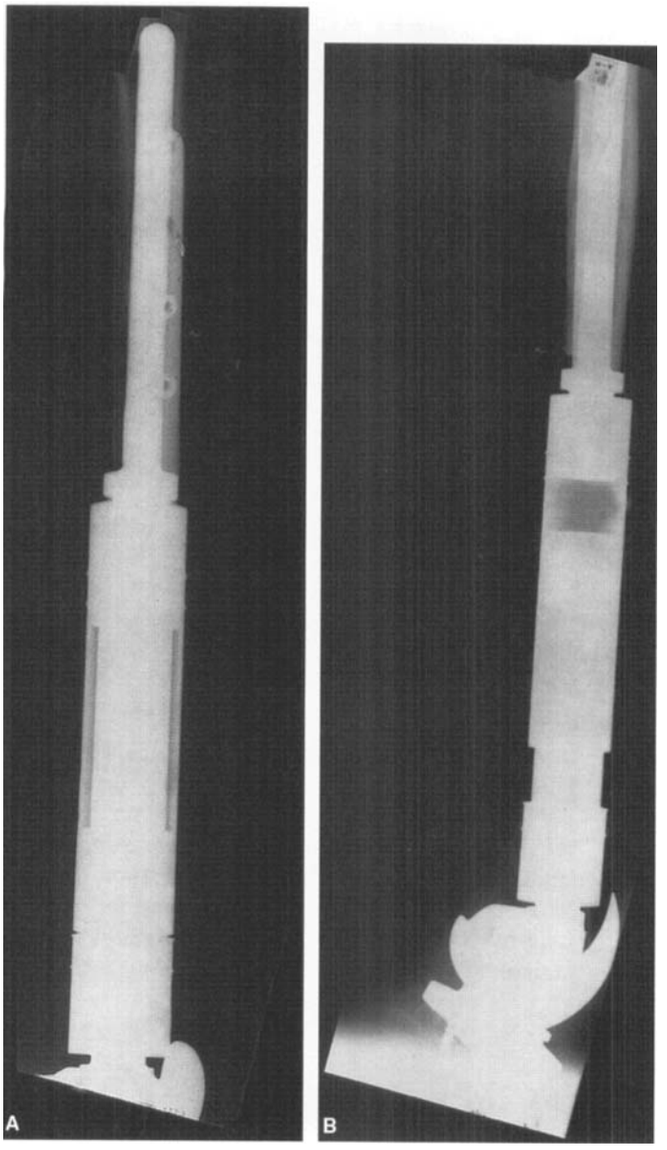

FIG. 5. X-rays demonstrating the growth of the endoprosthesis before the extensions **(a)** and after **(b)** are shown.

The operation followed a few weeks after chemotherapy. Local resection was possible because the neurovascular bundle was free of tumor and enough muscle tissue could be preserved. Resection was followed by reconstruction with the extendable endoprosthesis. Forty-eight hours after the operation, passive exercises were started. Active exercises followed gradually. Chemotherapy was resumed 3 weeks postoperatively and continued for 40 weeks. Eight months after the operation, a leg length discrepancy of 20 mm was estimated. Extensions of 5 mm were started and repeated every month to allow enough stress reduction in the soft tissue. X-rays before and after the extensions were taken to measure the increase in length.

Fifteen months after surgery an infected ingrown toenail caused infection of the endoprosthesis. The endoprosthesis was removed and replaced by a spacer surrounded by beads filled with antibiotics. The lengthening element was dismantled to check for signs of mechanical damage. Representative biopsies were taken for histological examination. Also, bacteriological cultures were prepared. Two months later, the patient died. Blood and bone marrow examination showed acute nonlymphocytic leukemia.

Results

Three months postoperatively, the patient was capable of stair climbing without crutches. High patient motivation resulted in a maximum flexion of

110 degrees and full extension. CT scans of the lungs showed no bone metastases. Six extensions were performed, resulting in 19.5 mm of growth. During the extensions, it was necessary to use a larger magnetic field and to change the leg position to decrease tension of muscles surrounding the endoprosthesis. After extirpation of the endoprosthesis, the elongation predicted from the x-rays was confirmed. Histologic examination of the tissue around the bellows showed no tumor, some atrophic muscle tissue, and a thin layer of granulation tissue; a bacteriological culture of the knee showed coagulase negative *Staphylococcus epidermidis.* Bacteriological culture of samples from inside the bellows was negative. Analysis of the prosthesis showed evidence of intensive use. The most important observations were as follows: First, there were signs of wear of the PTFE layer. In vitro tests showed the same signs caused by running-in effects. Measurements showed that the remaining thin layer sufficed in reducing friction forces as much as before implantation. Second, the bellows had partially loosened from the prosthesis because of a failed glue bond. The cleaning procedure was improved to restore optimal bonding. Even with a failed bond, all PTFE particles were contained. Third, play was found between 2 parts of the lengthening element. The amount of it and absence of any cracks eliminated deformation of the material as a cause. In the future, the 2 parts will be welded together. Fourth, moisture was found inside the inner tube despite 2 sealing rings. Corrosion of the outside of the gearbox was obvious. The moisture could be explained because one of the presurgical tests on watertightness had shown unexpected leakage. After repair of the area responsible for the leakage, the inside of the prosthesis had not been dried, and this resulted in the observed moisture. Fifth, the geometry of the 2 bearing discs of the internal magnet was changed from round to oval. Probably, internal stresses were activated by the high sterilization temperatures up to 230°C. In the manufacturing guidelines, preheating of the bearing discs and a test for geometry were added. The manufacturing problems had not caused improper functioning of the prosthesis. The manufacturing changes mentioned should be sufficient to guarantee successful further application of this lengthening element.

Discussion

Several lengthening systems have been applied in growing children; however, all of these systems must be adjusted invasively (8,9). The resulting increased infection risk will restrict their application. The presented endoprosthetis can be extended noninvasively and will allow a wider introduction of these systems.

The first clinical experience with the adjustable endoprosthesis has been successful although the prosthesis clearly showed signs of intensive use. Some assembling errors became apparent, but they did not impair function. Six extensions could be performed, resulting in 19.5 mm of extension. The patient regained almost normal function of his leg. The clinical research studies will be continued at the Groningen University Hospital. If the clinical multiple centers trials are successful as well, the Extendable Modular Endoprosthetic System will be introduced into the market.

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