Chapter 14
Worldwide Experience with the Cañadell Technique

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Abstract Cañadell's technique for limb preserving surgery in pediatric bone sarcoma treatment was developed at the *Clínica Universidad de Navarra* in Pamplona, Spain and first presented in 1984. Recently, teams at many hospitals all over the world (for example, in China, Switzerland, Brazil, the Netherlands, Germany, Hungary, and Turkey) have successfully used the technique and published their results. Only now is it becoming clear that the positive results reported by Cañadell

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at the beginning of the 1990s can be easily achieved by other experts in the field. To illustrate this point, we present here some of the results obtained with this technique by teams based in hospitals other than that of Cañadell in Pamplona

Keywords Bone sarcoma • Limb salvage • Epiphyseal preservation • Cañadell's technique • Cryosurgery • Recycled bone

14.1 Application of Cañadell's Technique in Four Chinese Hospitals

Cañadell's technique involving epiphysiolysis before tumor excision [1] in order to preserve the epiphysis in limb salvage surgery associated with treatment for malignant bone tumors in adolescents has been widely accepted and used in clinical practice all over the world. Since April 2010 and especially since the publication of the Chinese edition of "Pediatric Bone Sarcoma" [2] in December 2011, the technique has gradually been used more and more in China. We report on 15 patients who have undergone epiphysiolysis in four Chinese hospitals up to January 2015.

14.1.1 Methods

The four Chinese hospitals whose experiences are reported here are the General Hospital of Ji'Nan Military commanding Region (Ji'Nan, China)(JN), HeNan Cancer Hospital (ZhengZhou, China)(ZZ), TianJin Hospital (TianJin, China)(TJ), and XiJing Hospital (XJ) (Table 14.1).

In JN from July 2012 to October 2014, five patients were treated with epiphysiolysis before tumor excision; there were three boys and two girls, with median age of 8 years (6–11 years) at surgery. Three neoplasms were located in distal femur and two in proximal tibia. On the basis of the Enneking staging system [3], in all five patients the disease was in stage IIB. All tumors were pathologically diagnosed as osteosarcoma, with four being of the osteoblastic type and one of the chondroblastic type. Preoperative chemotherapy was given in two courses on a neoadjuvant basis with cisplatin, Adriamycin and ifosfamide [4]. The reconstruction methods after tumor resection were distraction osteogenesis in one patient, alcohol inactivated autograft replantation in one patient, and microwave inactivation with external fixation in three patients.

In ZZ, between April 2010 and November 2012 [5], five patients were treated with epiphysiolysis before tumor excision; there were two boys and three girls, with median age of 13 years (9–15 years) at surgery. All five neoplasms were located in left distal femur. On the basis of the Enneking staging system, disease was at stage IIB. All tumors were pathologically diagnosed as osteosarcoma. Preoperative chemotherapy, which was given twice on a neoadjuvant basis, was with methotrexate,

Table 14.1 General information of 15 patients in four Chinese hospitals

No.	Hospital	Birth	Age	Gender	MRI type	Epiphysiolysis surgery	Site	Resection surgery	Reconstruction method	Chemo	Follow-up (months)	MSTS	Limb length (L/R cm)	Compli-cation	Pathology
1.	JN	2001/4/21	11	Male	2	2012/7/11	Left proximal tibia	2012/8/2	Distraction osteogenesis	Cisplatin, adriamycin and ifosfamide	30	29	82/81	None	Osteo-sarcoma
2.	JN	2004/9/6	7	Female	2	2012/7/30	Left distal femur	2012/8/29	Alcohol inactivated autograft replantation	Cisplatin, adriamycin and ifosfamide	17	28	82/84	Autograft fracture	Osteo-sarcoma
3.	JN	2008/7/12	6	Female	2	2014/8/18	Right distal femur	2014/8/27	Microwave inactivation with external fixation	Cisplatin, adriamycin and ifosfamide	5	28	74/74	None	Osteo-sarcoma
4.	JN	2005/8/20	9	Male	2	2014/9/1	Right proximal tibia	2014/9/24	Microwave inactivation with external fixation	Cisplatin, adriamycin and ifosfamide	6	30	77/77	None	Osteo-sarcoma (chon-droblast)
5.	JN	2006/1/10	8	Male	1	2014/10/17	Left distal femur	2014/11/7	Microwave inactivation with external fixation	Cisplatin, adriamycin and ifosfamide	3	30	72/72	None	Osteo-sarcoma
6.	ZZ	1996/11/27	15	Female	3	2011/7/9	Left distal femur	2011/8/4	Allograft replantation	Methotrexate, pirarubicin, carboplatin and ifosfamide	41	23	69/69	Joint stiffness	Osteo-sarcoma
7.	ZZ	1994/9/1	15	Female	2	2010/4/30	Left distal femur	2010/5/13	Allograft replantation	Methotrexate, pirarubicin, carboplatin and ifosfamide	21	29	76/76	Pulmonary metastasis	Osteo-sarcoma

(continued)

Table 14.1 (continued)

No.	Hospital	Birth	Age	Gender	MRI type	Epiphysiolysis surgery	Site	Resection surgery	Reconstruction method	Chemo	Follow-up (months)	MSTS	Limb length (L/R cm)	Compli-cation	Pathology
8.	ZZ	2003/4/10	9	Female	1	2012/11/22	Left distal femur	2012/11/22	Inactivated autograft replantation	Methotrexate, pirarubicin, carboplatin and ifosfamide	21	25	58/58	Autograft nonunion	Osteo-sarcoma
9.	ZZ	1995/4/14	15	Male	1	2010/7/21	Left distal femur	2010/7/29	Allograft replantation	Methotrexate, pirarubicin, carboplatin and ifosfamide	54	24	70/74	Infection and allograft rejection	Osteo-sarcoma
10.	ZZ	1995/9/15	11	Male	2	2010/1/19	Left distal femur	2010/2/6	Allograft replantation	Methotrexate, pirarubicin, carboplatin and ifosfamide	59	29	81/84	Pulmonary metastasis	Osteo-sarcoma
11.	TJ	2004/9/1	9	Male	3	2013/9/23	Left distal tibia plus lung mets	2013/10/21	Distraction osteogenesis	Doxorubicin and cisplatin	17	18	Unknown	Recurrence and amputation	Osteo-sarcoma
12.	TJ	2008/1/30	6	Female	1	2014/5/16	Left distal tibia	2014/6/17	Distraction osteogenesis	Doxorubicin and cisplatin	7	22	Unknown	Delayed union	Ewing's sarcoma
13.	TJ	2006/1/5	8	Male	2	2014/8/14	Left distal femur	2014/9/10	Distraction osteogenesis	Doxorubicin and cisplatin	4	21	Unknown	Infection	Osteo-sarcoma
14.	TJ	2004/11/18	6	Male	1	2012/6/28	Right distal tibia	2012/8/20	Distraction osteogenesis	Doxorubicin and cisplatin	22	30	Equal	None	Osteo-sarcoma
15.	XJ	2003/8/12	8	Male	1	2012/5/25	Left proximal tibia	2012/6/21	Allograft replantation with pedicled fibula	Methotrexate, cisplatin, adriamycin and ifosfamide	26	30	Equal	Skin ulcer and local infection	Osteo-sarcoma

pirarubicin, carboplatin and ifosfamide. The reconstruction methods after tumor resection were inactivated autograft replantation in one patient, and allograft replantation with internal fixation in four patients.

In TJ from June 2012 to August 2014, four patients were treated with epiphysiolysis before tumor excision. The patients were three boys and one girl; median age at surgery was 7 years (6–9 years). One neoplasm was in the left distal femur, and three were in the proximal tibia. Three patients were in Enneking stage IIB; one boy was in stage III with pulmonary metastasis. The tumors of the three boys were pathologically diagnosed as osteosarcoma; the girl had a Ewing's sarcoma. Preoperative chemotherapy was doxorubicin and cisplatin, which were given in three courses on a neoadjuvant basis. The method chosen for reconstruction after tumor resection was distraction osteogenesis in all four patients.

In XJ, one 8-year-old boy with a neoplasm in his left proximal tibia received epiphysiolysis before tumor excision, in May 2012. Disease was at stage IIB and pathologically diagnosed as osteosarcoma. Preoperative chemotherapy was in three courses, on a neoadjuvant basis, and with methotrexate, cisplatin, Adriamycin and ifosfamide. The method chosen for reconstruction was allograft replantation with vascularized fibula.

All patients received postoperative courses of neo-adjuvant chemotherapy. The follow-up schedule involves revisions every 3 months in the first and second year, and then every 6 months for the next 3 years. Postoperative results were evaluated according to the MSTS limb function score system. Statistical analysis involved calculation of the correlation between related factors, survival, and postoperative function.

14.1.2 Results

In JN, after a mean follow-up of 12 months (3–30 months), all children were alive and four patients were disease-free. One girl experienced fracture of an inactivated autograft and required a second operation with internal fixation. This girl, who was 7 years old at the initial surgery, was the only of the patients to suffer any limb discrepancy. The other four children showed equal lower limb length of 82, 74, 77 and 72 cm [6] (Fig. 14.1). At the most recent follow-up, no cases of recurrence or metastasis were found, and the mean MSTS score was 29 (ranging between 28 and 30).

Of the ZZ patients, one died of pulmonary metastasis 6 months after start of treatment (epiphysiolysis). After a mean follow-up of 39 months (21–59 months), the other four children treated at ZZ were alive [5] but with certain complications: one girl had knee joint stiffness (30 months after epiphysiolysis); one boy was found to have pulmonary metastasis (31 months after epiphysiolysis (Fig. 14.2); one girl suffered non-union of an inactivated autograft, which required a second round of surgery with bone grafting (4 months after epiphysiolysis); and one boy suffered allograft infection (7 months after epiphysiolysis). The four surviving patients all have a degree of limb discrepancy: from 3 to 5 cm. At the most recent follow-up, no cases of recurrence were found, and the mean MSTS score was 26 (from 23 to 29).

In TJ, after a mean follow-up of 12 months (4–22 months), all four children were alive. One, a 6-year-old boy, had no recurrence, no complications, limb equivalence,

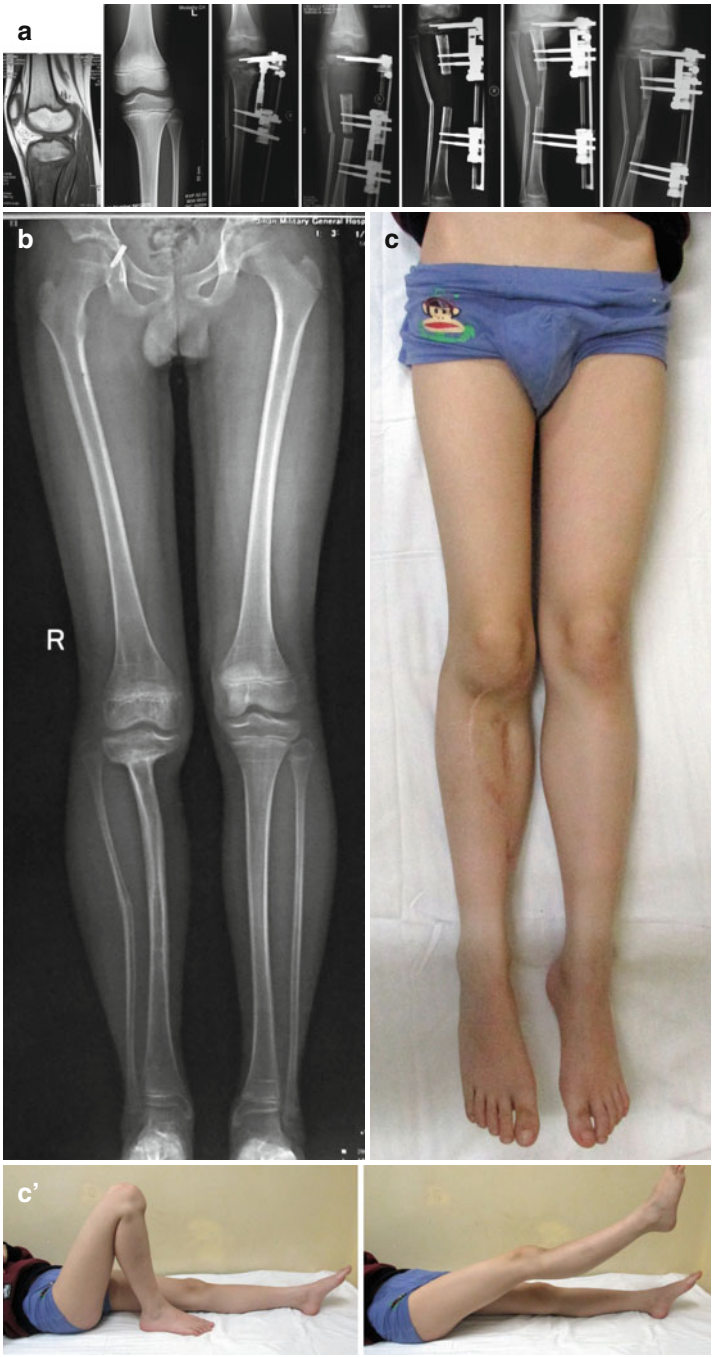

Fig. 14.1 (**a**) The preoperative MRI showed the tumor to be in contact with the physis. Physeal distraction was achieved, and reconstruction was made through bone transport. After 30 months, X-ray showed full bone union. (**b**, **c**) The boy showed limb equivalence with MSTS score of 30 (Endorsed by Pro.XiuChun Yu)

Fig. 14.2 (**a**) Eleven year boy. The preoperative MRI showed the tumor to be nearly in contact with epiphysis, classified as Type 2. After epiphysiolysis, the patient underwent tumor resection and allograft reconstruction. Twelve months later, X-ray study showed full bone union; After 29 months, pulmonary metastasis was detected; treatment was thoracoscopic resection of pulmonary nodule. After 54 months, (**b**–**d**) the patient was alive with no metastasis; lower limb discrepancy was 4 cm. MSTS score was 29 (Endorsed by Pro.QiQing Cai)

and an MSTS score of 30. One boy suffered tumor recurrence above the epiphysis and underwent a second operation, with above-knee amputation. One boy had wound infection (3 months after epiphysiolysis); limb length discrepancy has not been recorded. One, the girl, had delayed union of the distal tibia and limb length

discrepancy has not yet been recorded. At the most recent follow-up, the mean MSTS score was 23 (from 18 to 30).

After a follow-up of 26 months, the 8-year-old boy with OS treated at XJ was without recurrence, disease-free, and had limb equivalence. However, he experienced skin ulceration and local infection 1 year after the first operation and underwent further surgery to remove the internal fixation and perform transposition of the muscle flap. At the latest follow-up, the MSTS score was 30.

In summary, of the 15 patients, after a mean follow-up of 22 months (4–59 months), 12 (80 %) showed no evidence of disease, and eight (53 %) showed limb equivalence. Just one patient experienced local recurrence above the epiphysis. Seven patients (47 %) suffered complications, such as, skin ulceration, infection, delayed union, autograft fracture, and joint stiffness. Pooling evaluations of the most recent follow-ups, the mean MSTS score was 26.4, ranging between 18 and 30.

14.1.3 Discussion

The limb salvage procedure should not delay adjuvant therapy; reconstruction should be enduring and not be associated with a large number of local complications requiring secondary procedures and frequent hospitalization; and function of the limb should be at least as good as that obtained by amputation [7].

In most cases of osteosarcoma, especially in young patients, resection of a metaphyseal tumor with a 3–5 cm safe margin implies loss of the adjacent joint and such loss usually leads to limb length discrepancy. However, a safe margin in the context of a metaphyseal tumor can be obtained without sacrificing the epiphysis: as described by Cañadell, in tumors that do not cross the growth plate, physeal distraction provides a safe margin while averting loss of the epiphysis [2]. The growth cartilage itself is believed to provide a dependable margin of safety and so the 3–5 cm margin suggested by most authors is unnecessary.

The absence of anastomoses between epiphyseal and metaphyseal vessels means that in those cases where imaging methods indicate that the epiphysis has not been affected by the tumor, it is possible to conserve the epiphysis and the joint while resecting the tumor [2]. This is made possible by physeal distraction according to Cañadell's technique [1]. Note that physeal distraction is not used for bone lengthening, but rather as the first part of tumor resection: it effects a separation of the epiphysis from the tumor-bearing metaphysis.

The indications for physeal distraction in pediatric bone sarcoma treatment are that the tumor must be located in the metaphysis, that the physis must be open, and that the tumor must not have transgressed the physis. If the tumor is in contact with part of the physis, physeal distraction can be tried. MRI is the imaging method of choice in evaluating physeal tumor involvement, and enables categorization of tumors near the epiphysis into three types [8]. As described by San-Julian, if all of the physis is affected, there is a great possibility that tumor cells have passed across it and consequently physeal distraction is contraindicated [8]. Crucial factors in the

success of physeal distraction are a positive response to chemotherapy, accurate preoperative assessment of tumor extension to the epiphysis by MRI, and appropriate reconstruction techniques.

In the group of 15 patients reported here who underwent Cañadell's technique, 12 (80 %) experienced no recurrence or metastasis, and eight (53 %) showed limb equivalence. However, four patients (47 %) had recorded limb discrepancy of between 1 and 4 cm and for a further three patients (33 %) limb lengths were not recorded or not relevant. Differences may exist in the details of how epiphysiolysis was carried out in the four hospitals considered. Seven of the 15 patients (47 %) had complications, some of which may be associated with different reconstruction methods in the four hospitals. In general, for all patients, limb function was acceptable in the most recent follow-up; the mean MSTS score was 26.4 (18–30).

14.1.4 Conclusion

In China, Cañadell's limb salvage procedure involving epiphysiolysis before tumor excision for skeletally immature patients has gradually been adopted in clinical practice. All of the patients reported here, who were treated at four Chinese hospitals, can be seen to have benefitted from undergoing the technique. Naturally, variations in management of the technique and different reconstruction methods after tumor resection are expected to affect clinical results.

14.2 Preservation of Joints in Pediatric Diaphyseal and Metaphyseal Bone Sarcomas by Gradual Separation through the Physis. Management of Reconstruction Problems

14.2.1 Introduction

The artificial joint reconstructions currently available are prone to failure with time and are imperfect substitutes for natural biological joints. While diaphyseal bone structures can be anatomically reconstructed by relatively simple techniques and measures, the reconstruction of joints poses a much more complex problem. The goal in children and young people with normal life expectancy must be biologic reconstructions that can have lifelong durability.

In treating sarcomas it is crucial to remove the tumor completely, leaving no living tumoral cells within the body. How to achieve uncontaminated margins is one of the great challenges in tumor surgery, and how much distance is necessary between the surgical cut and the tumor being removed is a matter of debate. Without pathologic examination, delineation of tumor boundaries depends on the macroscopic

imaging techniques currently available. The decision of how much apparently healthy tissue to excise around a tumor ("wide" and "marginal" margins according to Enneking) is, unfortunately, in most cases still "experience based" if the dissection planes are not determined by anatomic structures (in which case "radical" margins are indicated according to Enneking).

Joint preservation depends primarily on preservation of the cartilaginous components of a joint. Ligaments can be partially reconstructed. To preserve a joint there are principally three possible resection planes:

- Metaphyseal resection with preservation of the physis. This is comparable to osteotomy.
- Trans-physeal resection by slow distraction. This is the so-called Cañadell technique or Pamplona technique (Canadell/San Julian 8, 9).
- Trans-epiphyseal resection.

Excellent results have been obtained with and reported for the Cañadell/Pamplona technique [8, 9] when appropriately indicated. Surprisingly, then, the approach is still regarded by some in the Americas and Europe as controversial; it has, however, received acceptance in China [10, 11].

We have used the Pamplona technique in six patients since 1988 and have not encountered any case of local recurrence. Our results were published in 2012 [12]. The technique has been applied when the growth plate was judged not to have been crossed by the tumor, even if the tumor was in contact with up to three quarters of the length of the growth plate. One patient in our series died from metastases, while all others continue to do well at the time of writing (April 2015). None had local recurrence. At 8-years follow-up, four patients have Musculoskeletal Tumor Rating Scale (MSTS) scores of 30 points, the other patient has a score of 25 points. In all cases the MSTS score excludes the point "emotional acceptance"; all patients, however, express complete satisfaction with their reconstructions in long term follow-up.

While we found the technique of physeal distraction reliable and useful, we have still had to struggle with the reconstruction and wish to discuss here several aspects of difficulty encountered in three patients.

14.2.2 Patients, Methods and Results

Patient 1. (N.S.; born in 1994; Fig. 14.3). A girl diagnosed with high-grade osteosarcoma at age 11 years (Fig. 14.3a). Despite her young age, the patient insisted on a wholly biologic reconstruction of her leg. To the treating staff physician, physeal distraction appeared to have progressed uneventfully. However, on reviewing all the images on the eve of surgery, the surgeons (the authors of this paper) recognized that laterally part of the physis had remained intact and a fracture through the tumor bearing metaphysis had occurred (Fig. 14.3b). Trans-epiphyseal resection was performed (Fig. 14.3c). The defect was reconstructed with free microvascular fibula transfer (Fig. 14.3d). The patient expressed satisfaction with her leg reconstruction, but died from systemic metastases (that had already been evident at the time of tumor surgery) 8 months later.

Fig. 14.3 (**a**) Patient 1. Osteosarcoma. The MRI shows the extent of the tumor, which is in contact with two thirds of the distal femoral physis. (**b**) This X-ray taken after 12 days of distraction for physeal separation shows the fracture through the metaphyseal part of the femur; part of the osteosarcoma remains attached to the epiphysis. (**c**) This intra-operative X-ray shows the K-wire placed for guidance of the saw between the K-wire and the Schanz screws used for fixation of the external distractor. (**d**) Postoperative documentation of the reconstruction with free microvascular fibula

Patient 2. (F.H.; born in 1995; Fig. 14.4). A 10-year-old boy diagnosed with high-grade osteosarcoma in the right femur (Fig. 14.4a) and treated in 2005. Chemotherapy was according to COSS 96. Physeal distraction was carried out (Fig. 14.4b). Initial reconstruction was with free microvascular double barrel fibula (Fig. 14.4c). Because of partial failure and lack of signs of bone formation, an allograft was added 8 months after the initial reconstruction, leaving part of the fibula (Fig. 14.4d). At age 14 years, the patient underwent epiphysiodesis for the contralateral knee. At the time of writing, the patient is 19 years old, disease free, has 130°-0°-0° flexion/extension of the knee, and a MSTS score of 30.

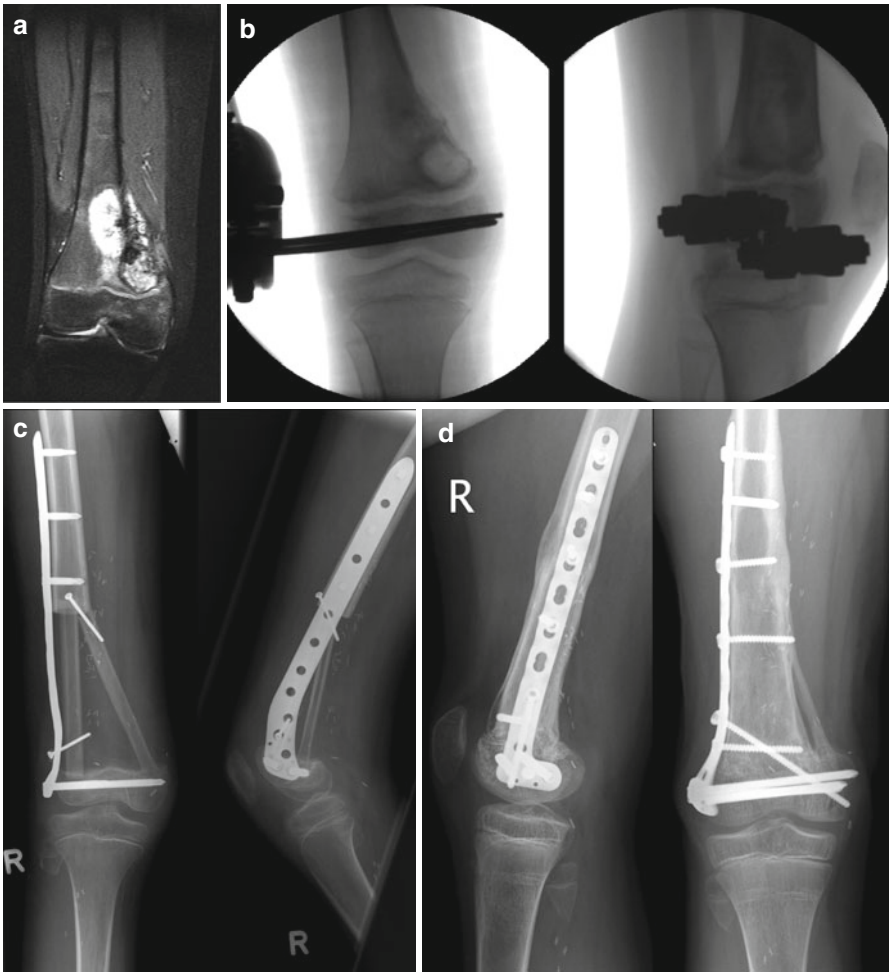

Fig. 14.4 (**a**) Patient 2. Osteosarcoma in the distal femur. MRI after preoperative chemotherapy. (**b**) Physeal separation before definitive surgery. (**c**) Post-operative X-ray after reconstruction with a free microvascular allograft. (**d**) Definitive healing after additional allograft

Patient 3. (R.K.; born in 1993; Fig. 14.5). A 15-year-old girl diagnosed with high grade osteosarcoma in the right femur (Fig. 14.5a). Chemotherapy was according to EURAMOS. Physeal distraction was carried out (Fig. 14.5b). The tumor was resected

Fig. 14.5 (**a**) Patient 3. MRI showing the extensive involvement of the region of the Hunter canal. (**b**) CT reconstruction after physeal distraction showing correct rupture of the physis. (**c**) Initial reconstruction with allograft and reconstruction of the femoral vessels with autograft from the contralateral *Vena saphena magna*. (**d**) Failed allograft due to low grade infection with *Staphylococcus epidermidis*. (**e**) Temporary cement spacer. (**f**) Vessel loop formed with ipsilateral vein for arterial and venous anastomosis of the free microvascular fibula. (**g**) Final stable biologic reconstruction with allograft and "onlay" vascular fibula

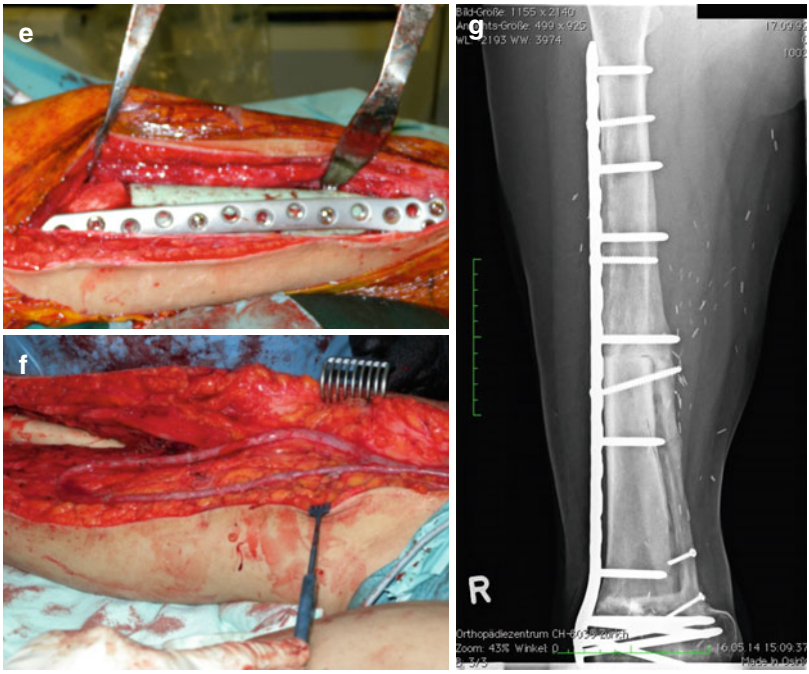

Fig. 14.5 (continued)

with the adjacent femoral vessels. Reconstructing of both the artery and vein was by contralateral saphenous vein graft. Reconstruction of the bone was with fresh frozen allograft (Fig. 14.5c). As a result of low grade infection with *Staphylococcus epidermidis*, the allograft did not fuse and fractured 3 years later (in 2010) (Fig. 14.5d). The allograft was removed and an antibiotic loaded cement spacer was implanted (Fig. 14.5e). Three weeks later the cement spacer was replaced by an allograft with simultaneous free microvascular fibula transfer using the initially preserved ipsilateral saphenous vein for arterial anastomosis to the femoral artery below the inguinal ligament (Fig. 14.5f). This allograft also failed and was replaced 3 years later (in 2013) leaving the transplanted fibula. This led to final definitive healing (Fig. 14.5g). Currently (2015), the patient is disease free and feels unlimited in spite of restricted flexion in the knee joint (flexion/extension is 110°-0°-0°). MSTS score is 25.

14.2.3 Discussion

The case of patient one, in which physeal separation was incomplete and fracture occurred in the tumor bearing metaphysis, illustrates the importance of careful analysis of the progress of physeal separation. If radiography is not unequivocally clear, it is necessary to consider using magnetic resonance (MRI) or computed tomography (CT) to assess whether separation has occurred within healthy bone. Note, however, that MRI is limited by the possibility of artifacts arising from the implants and device used for distraction.

In the case of patient two, because of the relatively short segment of excised bone and the young age of the patient, we opted for double barrel fibular reconstruction, which has greater potential for remodeling and thickening of the vascularized fibula. Subsequent secondary augmentation with an allograft resulted in full biologic healing, in spite of at the fact that there had been at least a partial failure of the initially transplanted fibula.

The situation in patient three was especially difficult because of the necessity at the time of tumor surgery to reconstruct not only the bone but also the arterial and venous vessels. In view of the complexity of the procedure, we considered it inappropriate to put at further risk the circulation in the extremity by augmenting the bone reconstruction with free fibula transfer. The failure of the allograft was most likely related to a low grade infection. The patient, who had chosen her biologic reconstruction, has persevered through many demanding reoperations and revisions but is finally satisfied with a fully biologically-reconstructed functional and stable leg.

14.2.4 Conclusion

Replacement of bone after tumor resection can be achieved through demanding procedures to establish biologic reconstructions or through relatively simple techniques with artificial implants. Apart from the much simpler and quicker procedures, another advantage of artificial implants is that rehabilitation is much shorter than that with biologic reconstructions. However, only biologic reconstructions have the potential to last for a lifetime; artificial reconstructions are prone to failure.

In our view, each patient is unique and the mode and material chosen for reconstruction must consider how to maximize potential future quality of life, that is, the quality added life years (QUALY) for the individual patient.

In carefully selected cases, the Cañadell or Pamplona technique of physeal distraction has contributed greatly to improve the long-term functional results in growing children subjected to resection of bone tumors. Whenever the technique is feasible, it should be considered.

14.3 The Experience in Brazil: Epiphyseal Distraction Combined with Autograft of Cryogenically Recycled Tumoral Bone. A New Method for Epiphyseal Sparing Surgery in Malignant Bone Tumors

14.3.1 Introduction

Patients with an open metaphysis and bone sarcomas that have not invaded the metaphysis can present a challenge to the orthopedic surgeon. In some cases, transepiphyseal resection osteotomy would not enable adequate future osteosynthesis because the remaining epiphyseal bone tissue would be too scarce, soft and thin.

The possibility of maintaining the epiphysis intact whilst maintaining (or even increasing) the resection margins through a previous separation of the diaphysis from the epiphysis was first described by Cañadell in 1984 and published in an international journal in 1994 [13]. Originally Cañadell and his co-workers reconstructed the bone defect with an autograft or an allograft. In Kanazawa, H. Tsuchiya and colleagues developed a simple method of recycling malignant bone tumor by freezing the specimen in liquid nitrogen; the method was described in 2005 [14]. We visited Kanazawa in 2004, and since then we have been using this method at our hospital. We have also had the opportunity to see San Julian presenting his technique at the ISOLS in Hamburg in 2007 and later also visited his department in Pamplona. Since then we have used, whenever indicated, these two techniques in combination. We have found no mention in the literature of this combined approach and, therefore, describe the method here.

14.3.2 Materials and Methods

From May 2008 to April 2010, three patients fulfilled the criteria for treatment by epiphyseal distraction and bone freezing. Epiphyseal distraction was undertaken following the descriptions of Cañadell and San Julian [8, 13, 15]. In all three cases we used a linear type LRS Orthofix external fixator inserting two pins proximally and two distally to the tumor limits. According to the tumor site, the two pins inserted at the epiphysis were always inserted parallel to the metaphyseal line. Fluoroscopy was used in all cases. Distraction started the day after placement, and separation of the epiphysis from the diaphysis took place around the 12th–14th day; the separation was felt by the patients, who referred pain and/or a click at the fixator. Definitive resection of the bone tumor was then scheduled.

The freezing technique consisted of en bloc excision of the tumor as a section of bone, removal of soft tissue, curettage of the medullary canal and any lytic part of the tumor and then incubation of the bone graft for 20 min in liquid nitrogen (the first 5 min intermittently and the other 15 continuously), thawing at room temperature for 10 min and finally thawing in distilled water for more 10 min. The graft was then ready to be re-implanted and fixed according to conventional osteosynthesis methods.

14.3.3 Case Reports

Case 1 (GSS)
This was a 12-year-old girl with a type IIB proximal right tibia osteosarcoma. The patient was sent to our hospital with pain in her right leg that had been ongoing for

almost 5 months. She had difficulty in walking and a growing mass. She had been radiographed at her town of origin, and referred directly to our unit when the X-ray revealed a huge bone tumor. Image based staging was performed, and 4 days later a biopsy was obtained to confirm the diagnosis. The X-ray and the MRI showed a huge bone mass, mostly extra-compartmental, growing to the medial side of the tibia but not crossing the metaphysis.

Neo-adjuvant chemotherapy was administered in accordance with the Brazilian protocol. Four months later, an external fixator was installed and distraction initiated; epiphyseal separation occurred on the 14th day. Two days later, the tumor was resected by means of a distal tibia osteotomy. The resected specimen was then treated in liquid nitrogen according to the Kanazawa protocol and re-implanted and fixed to the distal tibia diaphysis with two stainless steel plates and a spongiosa screw.

The extra compartmental tumor tissue was sent for pathological analysis; the report described it as extra-compartmental tumor tissue with possible viable tumor in regression. Almost 3 weeks later, adjuvant chemotherapy was started. Four months later, still on chemotherapy, the patient developed an infection at the distal site of osteotomy. The infection was treated with drainage and antibiotics and resolved easily, within 1 month. Nine months after tumor resection surgery, non-union was diagnosed at the distal osteotomy, and an iliac crest bone graft was performed.

During this period, the patient used an external articulated brace, which enabled her to put her full weight on her operated leg and enabled her to make active knee flexion and extension during gait and physiotherapy exercises.

Two years after tumor resection a solitary lung osteosarcoma metastasis was detected, and the patient underwent lung segmentectomy followed again by chemotherapy. Seven months after the lung operation, she developed another infection at the same site as the previous one. Five months later, local recurrence of the tumor was detected in the metaphyseal-diaphyseal area and the limb was amputated above the knee. Before amputation, despite all the complications, the patient had normal knee and ankle function. At the time of writing, 6 years after the initial tumor surgery, the patient is free of disease and walking with her lower limb prosthesis.

Case 2 (MFBS)

This is the case of an 8-year-old boy with a type IIB osteosarcoma in the distal right femur. The patient initially reported injury for 2 months and then pain. Finally, he could no longer walk. After biopsy and confirmation of diagnosis, neo-adjuvant chemotherapy was begun.

Three months later and after another biopsy, the case was evaluated for surgical planning. Although the radiologic evidence was not clear on one of the formal indications prescribed by Cañadell and San Julian [13, 15], epiphyseal distraction of the distal femoral epiphysis was considered opportune and a linear external fixator was installed. Separation occurred after 12 days of distraction. Five days later, the tumor was resected, the resected segment of bone was treated according to the Kanazawa

protocol, and the frozen autograft was re-implanted. Because the graft was too big and because, at that time, there was no adequate fixation system covered by the national health system, we were obliged to fix the graft with a straight stainless steel plate and two crossed screws distally.

Pathology analysis of the extra-compartmental tumor tissue found no viable tumor cells.

Consolidation at the distal site of reconstruction failed; this can be attributed to the inadequate fixation method and also, possibly, to the freezing of the bone. The original plate and screws were removed, and the non-union stabilized with an external brace that facilitated knee flexion and extension. A fibrous callus has since developed, and the patient is able to walk and do sports such as bicycle riding without the orthosis. He uses a shoe lift for discrepancy compensation. Knee function has been conserved. Currently, we are planning the placement of an external fixator to correct distal pseudo-arthrosis and to lengthen the femur.

Case 3 (IBB)
This was an 11-year-old boy with a stage IIB osteosarcoma in the distal left femur (Fig. 14.6). The patient reported pain for almost a year before he was X-rayed and the bone tumor was diagnosed. An incisional biopsy confirmed the diagnosis.

After finishing the conventional neo-chemotherapy protocol, and after establishing that the tumor had not invaded the epiphysis, epiphyseal distraction was undertaken. Separation occurred after 13 days.

Bone tumor resection was performed 7 days later. The resected segment of bone was then treated and frozen. The extra-compartmental tumor tissue sent to pathology revealed no viable tumor. The remaining bone was re-implanted and fixed with an angled stainless steel 90° plate.

Three weeks after being discharged from hospital, the patient was provided with an orthosis with knee and ankle flexion/extension; rehabilitation involved physiotherapy and walking with partial weight bearing.

Proximal and distal consolidation was observed in X-rays taken about 4 months after surgery, but the orthosis was maintained for 2 years as an external support to the plate and to avoid metal fatigue. At the time of writing, 6 years after the resection and reconstruction surgery, this patient has absolutely normal knee function and appearance of the knee is normal; there is only a slight growth reduction, of about 1.5 cm, in the operated leg. We plan to wait for the boy's skeletal maturation before removing the plate.

14.3.4 Results

All three patients were successfully submitted to epiphysiolysis before excision and separation occurred at an average time of 13 days. Graft consolidation to the host bone (as evaluated by X-ray) took an average of about 6 months to reach the status of being "good" (according to the ISOLS criteria regarding fusion of allografts (Table 14.2)).

In all cases, the long-term disadvantages of endoprosthesis substitution were avoided.

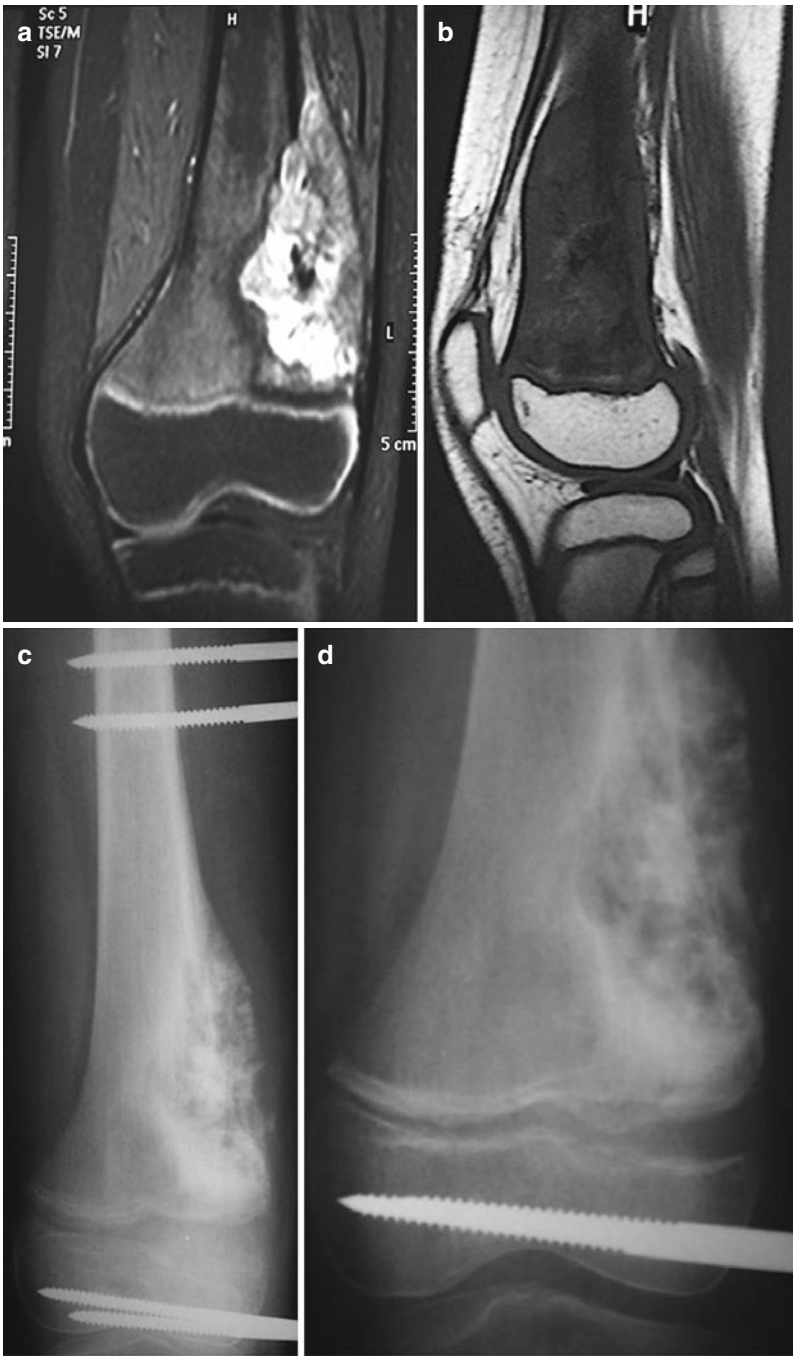

Fig. 14.6 (**a**, **b**) Stage IIB osteosarcoma. The epiphysis is preserved. (**c**, **d**) Epiphyseal separation. (**e**) Tumor specimen with extra compartmental tissue. (**f**) Remaining bone after dissection of extra compartmental tumoral tissue. (**g**) Frozen graft. (**h**) Post-operative X-ray showing fixation with 90° angled plate. (**i**) Four years post-op. (**j**, **k**) Six years post-op. Six years post-op., functional result with full weight bearing (**l**) and (**m**, **n**) normal knee flexion-extension

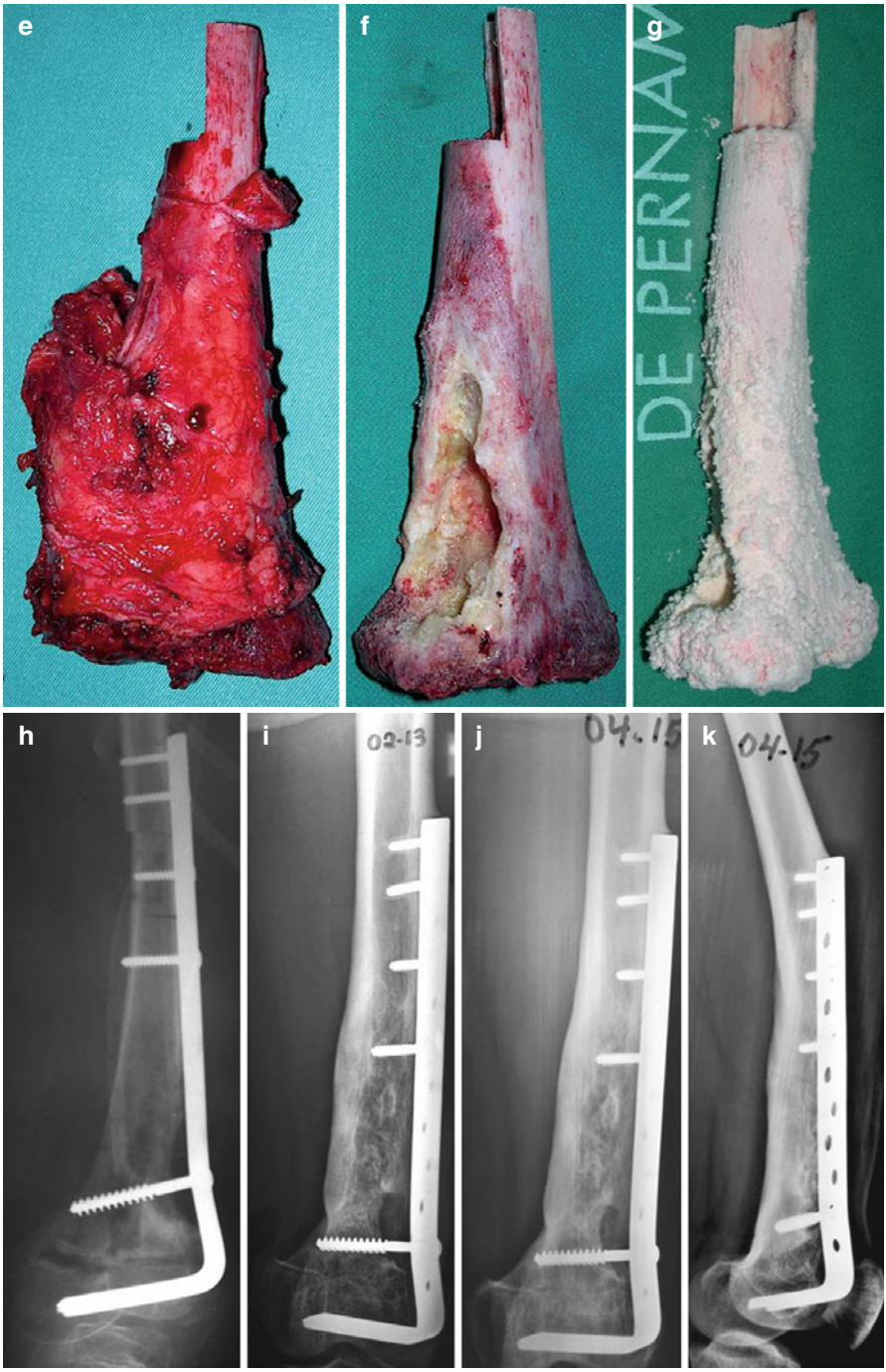

Fig. 14.6 (continued)

Fig. 14.6 (continued)

Table 14.2 ISOLS criteria regarding fusion of allografts

Excellent	Fusion complete. Osteotomy line not visible
Good	Fusion >75 %. Osteotomy line still visible
Fair	Fusion 25–75 %
Poor	Fusion <25 %. No evidence of callus

14.3.5 Discussion

Each of the three patients whose cases are described were operated on using exactly the same techniques and respecting the oncologic parameters for bone tumor surgery regarding margins. We followed the technique for epiphyseal distraction as described by Cañadell, and we followed the technique of biologic bone tumor reconstruction using recycled frozen bone as originally described by Tsuchiya.

We believe that local recurrence is neither related to epiphyseal distraction nor to the freezing method; local recurrence is absolutely related to the margins achieved during tumor resection. The higher incidence of recurrence in the leg can be attributed to the lack of soft tissue cover in the leg and extra-compartmental spread of tumors.

Unfortunately, we were unable to adhere completely to the principles of stable osteosynthesis because our public health system lacks provision for certain implants, and this limitation could explain the non-union in two of the cases reported here.

The combination of epiphysiolysis before tumor excision and reconstruction with recycled frozen bone as an autogenous graft constitutes a safe approach to the treatment of certain patients with bone sarcomas. The combination can preserve the growth potential of the limb in skeletally immature patients and provides the possibility of excellent long-term functionality.

14.4 Experience of the Hospital Vall d'Hebron of Barcelona

The aim of this commentary is to report the experience of the Hospital Vall d'Hebron of Barcelona with the surgical technique of physeal distraction before excision for the treatment of pediatric bone sarcomas as an alternative limb salvage procedure in skeletally immature patients.

At the Hospital Vall d'Hebron of Barcelona, from July 2006 to October 2013, five patients were treated by physeal distraction before tumor excision (Table 14.3); there were three girls (cases 1, 4 and 5) and two boys (cases 2 and 3). Age at the time of surgery was between 4 and 13 years (Figs. 14.7 and 14.8). All the tumors were located in metaphysis; three were in the proximal tibia (cases 1, 2 and 3), one was in the distal radius (case 4), and one in the proximal humerus (case 5). A histological diagnosis of Ewing's sarcoma was established in four patients (cases 1, 2, 4 and 5) and of osteosarcoma in one (case 3). Neoadjuvant chemotherapy was given to all patients.

The first surgical procedure, attaching the external fixator, involved the insertion of two pins into the epiphysis and another two into the diaphysis at least 4 cm from the diaphyseal tumor margin. The external fixator was then attached. In three cases we used a Blue Monotube (cases 1, 2 and 3) and in two cases a Yellow Monotube (cases 4 and 5). Distraction began in the operating room and was continued at a rate of 0.75–1 mm daily until rupture of the growth plate, which manifested with local pain and was confirmed by radiographic control.

The reconstruction methods after tumor resection were vascularized fibular free flap in one patient (case 1), intercalary bone allograft in three (cases 2, 3 and 5) and contralateral fibular autograft in one (case 4). After reconstruction, we maintained the external fixator in its place in four patients (cases 1, 2, 4 and 5). In one case (case 3), a medial gastrocnemius flap was transferred anteriorly, to cover the intercalary bone allograft.

Histological examination of the resection specimen confirmed in all cases that the margins were negative and also that the tumor had not involved the growth plate margins.

There were no cases of local recurrence in the retained epiphysis, but one patient (case 5) is currently undergoing chemotherapy treatment in another institution after local soft tissue recurrence and lung metastasis that was detected 14 months after the operation. At present, the rest of the patients (cases 1, 2, 3 and 4) are being followed up at our center, show no evidence of disease, and have excellent radiological and functional outcomes.

The patients presented the following orthopedic complications. Two patients with proximal tibial tumor (cases 1 and 2) suffered non-union of the graft that required a further operation to achieve union between the allograft and the host bone. One patient (case 1) had a 6 cm limb length discrepancy 85 months after surgery, and this disparity was resolved by contralateral epiphysiodesis with "8" plates. The patient with a tumor in the distal radius (case 4) suffered a fracture of the united allograft, which has been successfully treated by exchange osteosynthesis and autologous graft.

We believe that what has enabled us to apply the technique of physeal distraction before excision for the treatment of pediatric bone sarcomas with satisfactory results

Table 14.3 General information of the five patients of the Hospital Vall d'Hebron of Barcelona

No.	Birth	Age	Gender	Epiphysiolysis surgery	Site	Resection surgery	Reconstruction method	Chemo	Follow-up (months)	Limb length (R/L cm)	Complication	Pathology
1.	2003/7/16	4	Female	2007/10/18	Right proximal tibia	2007/11/12	Vascularized fibular free flap	VIDE VAC	89	73/79	None	Ewing
2.	1999/12/2	9	Male	2009/7/23	Right proximal tibia	2009/8/10	Intercalary allograft	VIDE VAC	60	84/85	Delayed union	Ewing
3.	1999/3/14	13	Male	2013/1/7	Right proximal tibia	2013/1/28	Intercalary allograft	Cisplatin, adriamycin and methotrexate	25	91/93	Soft tissue recurrence	Osteosarcoma
4.	2006/7/15	6	Female	2013/5/31	Left distal radius	2013/6/13	Contralateral fibular autograft	VIDE VAC	24	–	Autograft osteolysis	Ewing
5.	2008/10/22	5	Female	2013/10/10	Left proximal humerus	2013/11/14	Intercalary allograft	VIDE VAC	20	–	Autograft fracture	Ewing

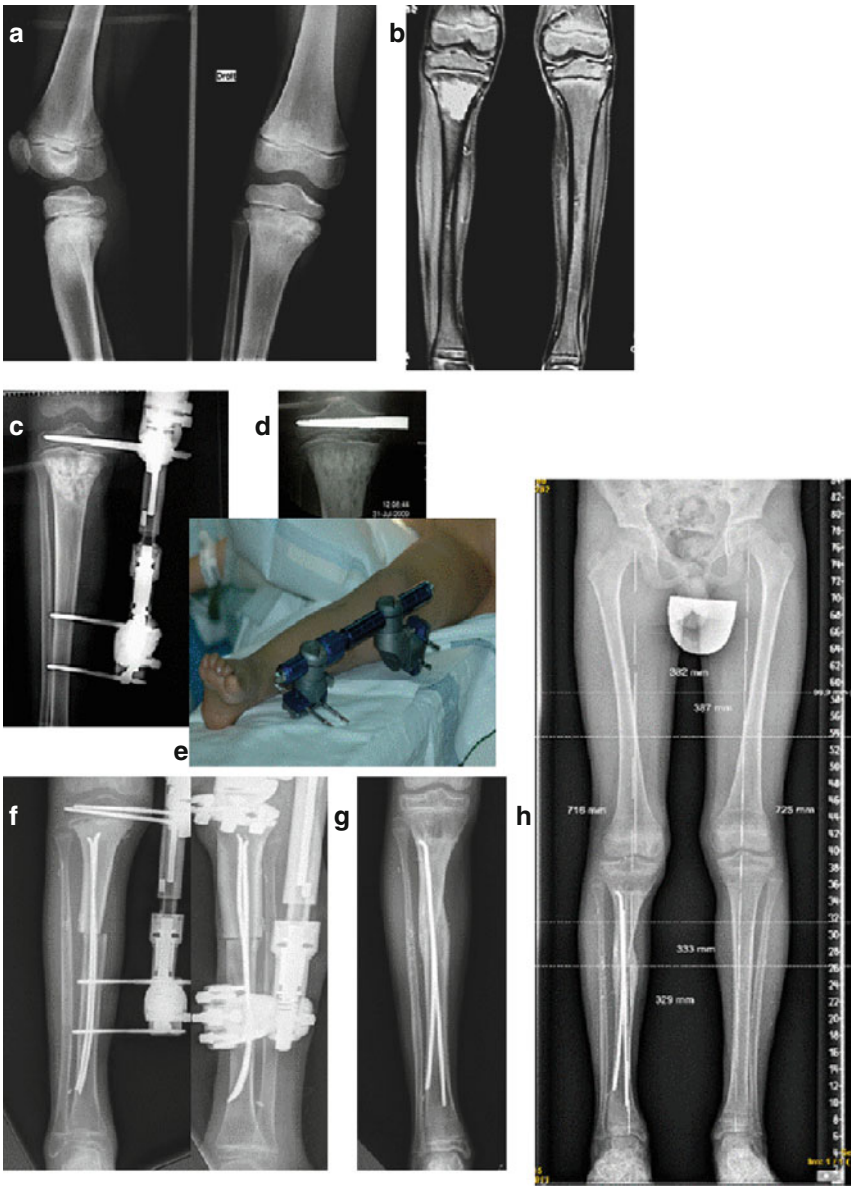

Fig. 14.7 (**a**, **b**) X-ray and MRI of a Ewing's sarcoma in the proximal tibia of a 9-year-old boy. (**c**–**e**) Physeal distraction before excision. (**f**, **g**) After reconstruction with an intercalary bone allograft. The growth plate in this patient currently remains active (**h**), 60 months after surgery

in our center is the combining of the expertise of specialists in pediatric orthopedics and in orthopedic oncology. We usually kept external fixation in place until consolidation of the bone graft with the epiphysis; this did not result in complications. Although the main goal of physeal distraction before excision is to preserve the

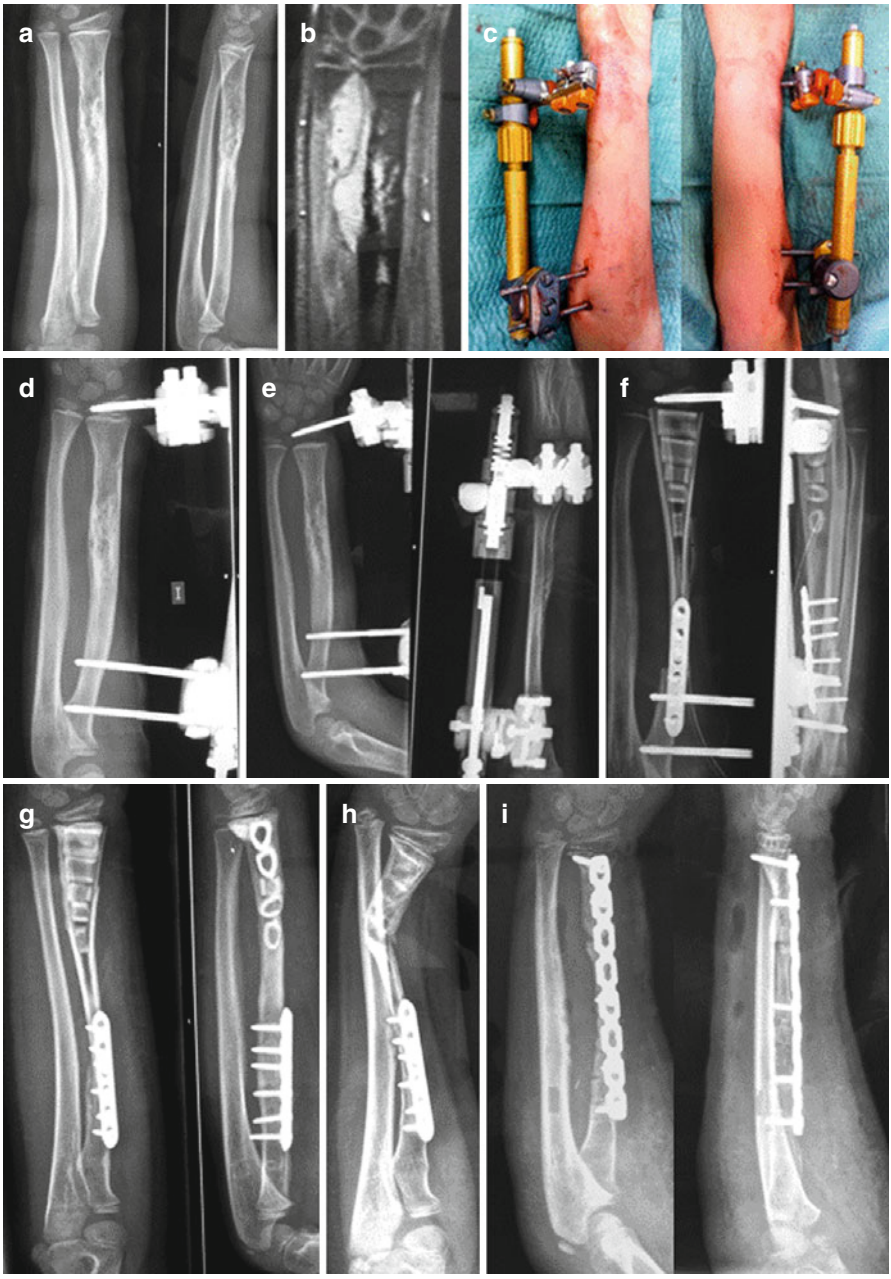

Fig. 14.8 (**a**, **b**) X-ray and MRI of a Ewing's sarcoma in the distal left radius of a 6-year-old girl. (**c**–**e**) Physeal distraction before excision. (**f**) After reconstruction with a contralateral fibular autograft. (**g**) Union of the autograft with active growth plate 6 months after surgery. (**h**, **i**) Fracture of the graft and treatment of this fracture

epiphysis and thus the joint, we have found that a low rate of distraction allowed us to maintain growth capacity in some of our patients. Consequently, the technique has enabled us to obtain good functional outcome for the joint and also a reduced degree of limb discrepancy.

References

1. Canadell J, Forriol F, Cara JA. Removal of metaphyseal bone tumours with preservation of the epiphysis. Physeal distraction before excision. J Bone Joint Surg. 1994;76(1):127–32.
2. Cañadell J, San-Julian M, Cara JA, et al. Conservation of the epiphysis while removing metaphyseal bone tumours: epiphysiolysis before excision. In: Cañadell J, San-Julian M, editors. Pediatric bone sarcomas: epiphysiolysis before excision. New York: Springer; 2009. p. 101–8.
3. Enneking WF, Dunham W, Gebhardt MC, Malawer M, Pritchard DJ. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. Clin Orthop Relat Res. 1993;286:241–6.
4. Xu M, Xu SF, Yu XC. Clinical analysis of osteosarcoma patients treated with high-dose methotrexate-free neoadjuvant chemotherapy. Curr Oncol. 2014;21(5):e678–84.
5. Yao W, Cai Q, Gao S, et al. Epiphysis preserving operations for the treatment of lower limb malignant bone tumors. Eur J Surg Oncol. 2012;38(12):1165–70.
6. Xu SF, Yu XC, Xu M, et al. Successful management of a childhood osteosarcoma with epiphysiolysis and distraction osteogenesis. Curr Oncol. 2014;21(4):658–62.
7. Simon MA. Limb salvage for osteosarcoma in the 1980s. Clin Orthop Relat Res. 1991;270: 264–70.
8. San-Julian M, Aquerreta JD, Benito A, et al. Indications for epiphyseal preservation in metaphyseal malignant bone tumors of children: relationship between image methods and histological findings. J Pediatr Orthop. 1999;19(4):543–8.
9. Cañadell J, de Pablos J. Breaking bony bridges by physeal distraction. A new approach. Int Orthop. 1985;9:223–9.
10. Weitao Y, Qiqing C, Songtao G, Jiaqiang W. Epiphysis preserving operations for the treatment of lower limb malignant bone tumors. Eur J Surg Oncol. 2013;38:1165–70.
11. Zhang P, Feifei F, Qiqing C, Weitao Y, Songtao G, Wang J, Wang X. Effects of metaphyseal bone tumor removal with preservation of the epiphysis. Exp Ther Med. 2014;8(3):567–73.
12. Betz M, Dumont CE, Fuchs B, Exner GU. Physeal distraction for joint preservation in malignant metaphyseal bone tumors in children. Clin Orthop Relat Res. 2012;470(6):1749–54.
13. Cañadell J, Forriol F, Cara JA. Removal of metaphyseal bone tumours with preservation of the epiphysis. Physeal distraction before excision. J Bone Joint Surg Br. 1994;76:127–32.
14. Tsuchiya H, Wan SL, Sakayama K, Yamamoto N, Nishida H, Tomita K. Reconstruction using an autograft containing tumour treated by liqid nitrogen. J Bone Joint Surg (Br). 2005;87-B: 218–25.
15. Cañadell J, Forriol F, Cara JA, San-Julian M. Removal of metaphyseal bone tumors with preservation of the epiphysis. Physeal distraction before excision. In: Cañadel J, San-Julian M, Cara JA, editors. Surgical treatment of malignant bone tumors. Pamplona: Ediciones Universidad de Navarra; 1995. p. 153–60.