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Review

Musculoskeletal Sarcomas in the Forearm and Hand: Standard Treatment and Microsurgical Reconstruction for Limb Salvage

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Abstract. *Sarcomas in the forearm and hand are very rare, accounting for less than 1% of all upper-limb tumors and clinical outcomes after surgery and adjuvant therapies are uncertain. The forearm and hand present specific challenges due to their unique anatomical structures. There is little soft tissue and each compartment is narrow, such important structures exist in close proximity. Anatomic constraints make it difficult to achieve wide surgical margins. Although sarcomas often metastasize to the lung, the overall survival rate is excellent. Wide marginal resection during initial surgery is the most predictive factor for tumor control. The role of reconstructive surgery following wide excision for sarcoma of the forearm and hand is even more important than elsewhere in the body because excision is likely to cause bone, tendon and nerve defects, leading to severe functional deficits. Multiple options exist for bony and soft tissue reconstruction of the upper limb, with the choice dependent upon tumor type, wound characteristics, surgeon preference and the patients' functional requirements. Success should be measured not just by stable wound coverage but also by preservation of patient's health, limb cosmesis, sensation and function. Careful preoperative planning with consideration of all the possible resected structures should improve patient outcomes.*

Local control of sarcoma is best achieved by adequate resection at the primary tumor stage (1). However, the forearm and hand present specific challenges due to their unique anatomical structures. There is little soft tissue and each compartment is narrow and important structures exist in close proximity (2). Anatomic constraints make it difficult to achieve wide surgical margins. Tumors of less than 5 cm that are located in extremities elsewhere, are commonly localized to a single compartment, but this is rare for the forearm and hand (3). Complex functions of the hand are directly impacted by the sacrifice of important structures (Figure 1). Although some authors have previously described surgical treatments and outcomes for soft tissue sarcomas in the upper limb, challenges remain in defining adequate surgical margins and appropriate reconstruction (4-10).

In the present study, we review oncological and functional outcomes for patients with sarcoma of the forearm and hand. The focus of this review article is to discuss standard treatment and the role of microsurgical reconstruction in achieving functional restoration following limb salvage surgery.

Anatomical Consideration of the Distal Upper Extremities

The forearm and hand comprise unique anatomical structures. There are 19 muscles in the forearm, out of which 11 are classified as extensor muscles and eight belong to the flexor group. The forearm is one of the few places in the body where most muscles run in close vicinity to one another and almost in parallel. Most of the muscles originate close to the elbow and extend all the way to the tips of the fingers. The flexor tendons move 3-4 cm longitudinally during flexion and extension. Any grasping, lifting, holding or cupping motion is accomplished by the flexors. The flexor muscles are also responsible for bending the wrists downwards. Several other muscles assist in twisting motions of the forearm. The three major nerves are the median, ulnar and radial, while the two major arteries are the radial and ulnar. The intrinsic muscles of the hand are located in palmar and are innervated by either the median or ulnar nerve (2).

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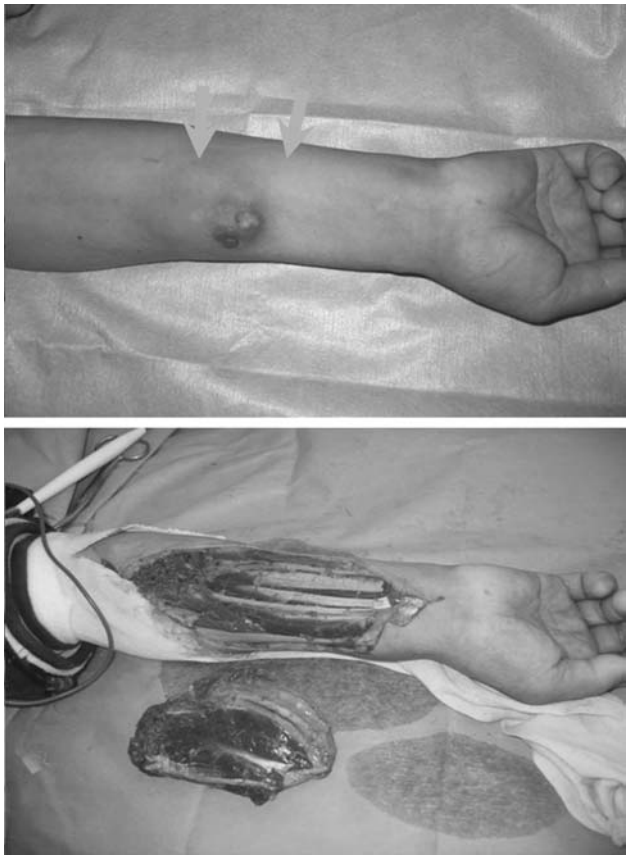

Figure 1. *A 61-year-old male with malignant fibrous histiocytoma in the palmar forearm. The forearm and hand present specific challenges due to their unique anatomical structure. Wide surgical resection directly causes significant functional loss because there is little soft tissue and each compartment is narrow, such that important structures exist in close proximity.*

Soft-tissue sarcomas arising in the hand or forearm are usually small lesions detected at a relatively early stage due to the paucity of soft tissue in this region. Despite their small size, sarcomas of the hand and forearm tend to be aggressive and are sometimes fatal (11).

Histological Subtypes of Sarcoma of the Distal Upper Extremities

Tumors of the forearm and hand are quite rare and are usually benign. Malignant tumors account for <3% of all upper limb tumors, with sarcomas accounting for <1%. Lohman *et al*. treated 100 patients with soft-tissue sarcoma in the upper extremity (8). The histological types were malignant fibrous histiocytoma (MFH) in 48% of cases, synovial sarcoma in 11% and liposarcoma in 8%. Similarly, Kim *et al*. presented 81 cases with osseous and soft tissue sarcomas out, of which MFH comprised 17%, osteosarcoma 10%, synovial cell sarcoma 7% and liposarcoma 6% of cases (6). Talbot *et al*. presented 55 cases with soft tissue sarcomas of the hand, including nine epithelioid sarcomas, eight MFH, six synovial sarcomas and three liposarcomas (12).

In the studies mentioned so far, the most common histological types appear to be MFH (40%), liposarcoma (15%) and synovial sarcoma (10%). Osseous sarcoma of the forearm and hand is even rarer than soft tissue sarcoma and accounts for about 0.5% of all malignancies in this area and 6% of benign osseous lesions. Chondrosarcoma is the most common sarcoma of the upper limb, especially of the hand (3).

Oncological Outcomes for Sarcomas in the Distal Upper Extremities

The clinical outcome for sarcomas located in the distal extremities is generally thought to be better than for sarcomas arising in the trunk wall. However, only a few studies have focused on sarcoma of the forearm and hand, and hence there is lack of reliable data (Table I).

Popov *et al*. demonstrated a 5-year overall survival rate of 75% and a 5-year metastasis-free survival rate of 68% in 80 patients with soft-tissue sarcoma of the upper extremities (7). Lohman *et al*. reported that 66% of cases showed no evidence of disease relapse after 31 months of follow-up (8). Gustafson and Arner reported a 5-year metastasis-free survival rate of 72% in 108 patients (13), while Kim *et al*. reported a 5-year survival rate of 61% in 71 patients (5).

Daecke *et al*. described the clinical outcome of 33 patients with osteosarcomas of the peripheral upper extremities (14). The 5-year survival rate was 86% and the event-free survival rate was 65%. In a study by Talbot *et al*., only three out of 55 (5%) patients with hand sarcoma died because of their tumor (12). Ramanathan *et al*. collected data on 110 patients with extremity sarcomas and found no significant difference in the clinical outcome of cases with upper *vs*. lower limb sarcoma, nor between proximal and distal extremity sarcomas (15).

We reviewed 26 patients with osseous and soft-tissue sarcomas, of which 19 were pathologically classified as high-grade tumor and 7 as low-grade. At the time of final follow-up, 22 patients (85%) had no evidence of tumor and two were alive with disease. One patient who had presented with pre-existing lung metastasis died of angiosarcoma 38 months after surgery and another patient died of epithelioid sarcoma of the forearm. The 3-year disease-specific survival rate was 100% and the 5-year rate was 88%, thus demonstrating a good clinical outcome in our series.

Indications for Chemotherapy

It remains controversial as to whether neoadjuvant and adjuvant chemotherapy are indicated for patients with sarcoma of the distal upper extremities. To our knowledge, there have not been

Table I. *Oncological outcomes for sarcomas in the upper extremity.*

Author (year) (ref)	Tumor	N	Chemotherapy (%)	5-year Overall survival (%)	5-year Disease-free survival (%)
Gustafson *et al*. (1999) (13)	Soft tissue (shoulder to hand)	108	11 (10)	Not documented	72
Lohman *et al*. (2002) (8)	Soft tissue (shoulder to hand)	100	27 (27)	82	66
Popov *et al*. (2004) (7)	Soft tissue (shoulder to hand)	80	Not documented	75	68
Kim *et al*. (2004) (5)	Soft tissue (shoulder to hand)	81	36 (44)	82	67
Dacke *et al*. (2005) (14)	Osteosarcoma	33	24 (72)	86	65
Talbot *et al*. (2006) (12)	Sarcoma in the hand	55	4 (7)	95	Not documented
Our series	Sarcoma in the forearm and hand	26	8 (31)	92	84

any publications to demonstrate significant benefit from adjuvant chemotherapy, especially in patients with soft-tissue sarcoma.

In the study of Lohman *et al*., only 27% of patients with soft-tissue sarcoma received neoadjuvant chemotherapy, 13% received adjuvant chemotherapy and 7% received both. Only 5% received chemotherapy in the study of Talbot *et al*. (12). Daecke *et al*. reviewed 33 patients with osteosarcoma treated with neoadjuvant and adjuvant chemotherapy in combination with wide resection of the tumor (14). They reported on a remarkably high rate of patient's survival using multi-agent chemotherapy.

Indication for chemotherapy should be considered in conjunction with tumor staging (16). The American Joint Committee on Cancer (AJCC) staging system can be applied to both sarcomas of the bone and soft tissue (17, 18) (Table II). The stages in this system are based on four factors: histological grade, tumor size (more or less than 5 cm), location (superficial or deep) and metastasis (lymph node or distant). We suggest that an AJCC tumor stage of III or more is an indication for neoadjuvant and adjuvant chemotherapy. Patients with high-grade tumors, tumor size larger than 5 cm, location in the deep layer, or distant metastasis are indicated for adjuvant chemotherapy. Osteosarcoma is commonly staged as greater than III and therefore indicated for chemotherapy.

The most commonly used anti-tumor agents for soft-tissue sarcoma are adriamycin, ifosfamide and cisplatin. The neoadjuvant chemotherapy regimen we use for soft-tissue sarcoma includes high-dose ifosfamide and adriamycin, while for osteosarcoma, it includes high-dose methotrexate, cisplatin and adriamycin (19).

Table II. *American Joint Committee on Cancer staging system (6th edition) for sarcomas of the bone and soft tissue.*

Stage	Grade	Primary tumor	Node	Metastasis
I	G1-2	T1a-b, T2a-b	N0	M0
II	G3-4	T1a-b, T2a	N0	M0
III	G3-4	T2b	N0	M0
IV	Any G	Any T	N1 N0	M0
	Any G	Any T		M1

AJCC TNM Classification for soft tissue sarcoma

Primary tumor (T)	T1 <5 cm in greatest dimension; T1a superficial, T1b deep T2 >5 cm; T2a superficial, T2b deep
Histological grade (G)	G1 Well-differentiated G2 Moderately-differentiated G3 Poorly-differentiated G4 Poorly or undifferentiated
Regional lymph nodes (N)	N0 No regional lymph node metastasis N1 Regional lymph node metastasis
Distant metastasis (M)	M0 No distant metastasis M1 Distant metastasis

Adequate Surgical Margins

Recommendations for safe surgical margins in the treatment of forearm and hand sarcomas are still vague and depend on tumor size, location and histological grade (20). Popov *et al*. reported a higher local recurrence rate of sarcomas of the upper limb compared to those of the lower limb, even though the mean tumor size was smaller in the upper limb (7). This probably reflects the fact that determination of adequate surgical margins is more difficult to achieve in the upper extremity because of the unique anatomical structures.

Surgical margins should never be sacrificed in an attempt to maintain hand function (21). Talbert *et al*. reviewed 78 patients with soft tissue sarcoma in the distal extremity and recommended 1-cm wide margins and radiation therapy (22). Bray *et al*. reviewed 25 patients with sarcoma of the forearm and hand and recommended >1 cm margins but without radiation therapy (23). The efficacy of radiation therapy has yet to be proven (15). Our strategy is 2-cm wide margins for high-grade soft-tissue sarcomas and 1 cm margins for low-grade bone tumors. Major nerves are preserved if margins are kept to 1 cm width. Local control is best achieved by adequate

Figure 2. *A 65 year-old-female with malignant fibrous histiocytoma in the palmar forearm. The tumor was treated with wide resection of the flexor muscles and reconstructed by functional gracilis muscle transfer. She can grasp her fingers strongly due to the re-innervated gracilis muscle.*

treatment of tumors in the primary stage (24). In our series, local recurrence was very low (2/18, 11%) in patients who presented with a primary tumor. Three patients with MFH showed recurrence, probably because of aggressive invasion into the subcutaneous tissue. This type of MFH has been well-documented by Fanburg-Smith *et al*. (25) and Matsumoto *et al*. (26) as an infiltrative subtype and a wider margin is required at the initial resection to entirely excise the lesion.

Microsurgical Reconstruction for Massive Soft Tissue and Osteochondral Defects (Table III)

Selection of cutaneous flaps. Careful strategic planning of the surgical procedure is mandatory in order to achieve functional reconstruction of the upper extremity, following tumor resection (27). Wide resection for sarcoma can entail large, deep and complex defects, particularly in patients with advanced-stage lesions. The large volume of the wound and the exposure of important structures such as nerves, vessels, tendons and bone can often necessitate free-tissue transfer. Immediate reconstruction using free-tissue transfer has many advantages compared with conventional wound closure (28). However, only a few articles have described the role of microsurgical reconstruction following resection of sarcomas in the forearm and hand (4, 6, 8, 9).

Earlier studies reported that microvascular tissue transfer and pedicled flaps produced similar functional results (5). In our experience, the pedicled radial forearm flap was a good choice for cases where the major arteries and muscles had not been sacrificed after wide resection (3). Free cutaneous flaps are indicated when the major arteries need to be sacrificed. Free flaps can provide a larger volume of durable and well-vascularized tissue than local or regional flaps. Several options for cutaneous flaps include anterior thigh flap, scapular flap and groin flap (11, 29). Complications in our series were rare and no infections or residual wounds were experienced.

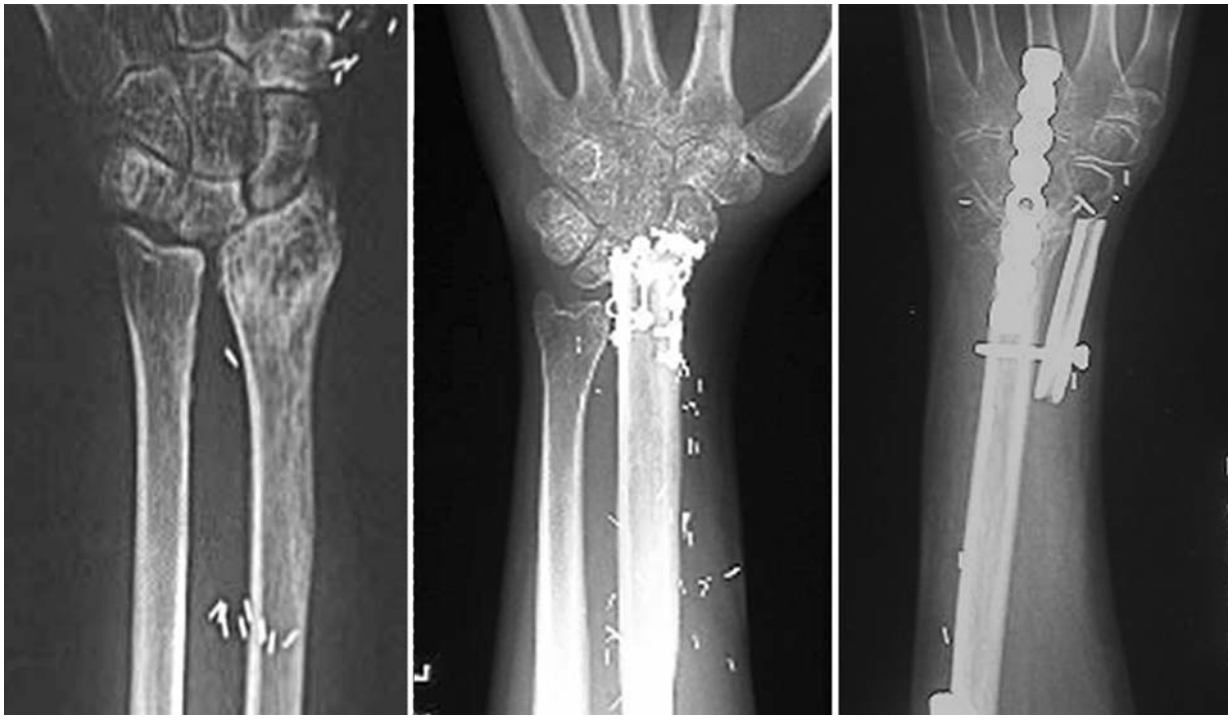

Figure 3. *There are three types of reconstruction of radio-carpal joint using free vascularized fibula graft, arthroplasty (left), and partial (middle) and total arthrodesis (right). If the carpal bones can be preserved, arthroplasty using the fibula head is recommended who are patients of non-heavy manual workers. Proximal carpal arthrodesis should be considered for young patients with high daily activity.*

Table III. *Forearm reconstruction after oncological resection.*

Defect tissue	Recommended reconstructions	
	Small defect	Large defect
Skin and subcutaneous	Skin graft (superficial)	Cutaneous flap (many candidates)
Muscle	Tendon transfer	Functional muscle transplantation (*gracilis* or *latissimus dorsi*)
Major nerve	Conventional nerve graft (<8 cm)	Vascularized sural nerve graft with peroneal flap (>8 cm)
Intercalary bone	Conventional bone graft	FVFG (or scapula, iliac crest etc) with peroneal flap
Osteochondral	Osteochondral auto or allograft	FVFG with partial or total wrist fusion
		Arthroplasty using vascularized fibula head
		Devitalized osteochondral autograft
		Osteochondral allograft

FVFG: Free vascularized fibula graft.

Neuro-vascularized muscle transfer. Functional neuro-vascularized muscle transfer (FMT) is a beneficial tool for restoring joint movement in cases involving the reconstruction of movement in the affected extremity (28, 30, 31). So far, the clinical application of FMT has been limited mainly to trauma cases (32-34). To our knowledge, there are no published studies on FMT for oncological reconstruction in the forearm, other than from our own work (35, 36). The gracilis muscle is best indicated for FMT (29, 36) (Figure 2). Two of our cases underwent entire resection of the finger extensor and flexor and were treated by FMT using the gracilis muscle. The muscle power recovered to grade 3. Another case underwent entire forearm extensor resection of the tumor and was reconstructed using the *latissimus dorsi* with a large cutaneous flap. However, the recovery of muscle power was excessive and balance of the flexor muscle was poor. Functional reconstruction of a limited muscle defect is usually an indication for tendon transfer and donor candidates exist in the forearm (37).

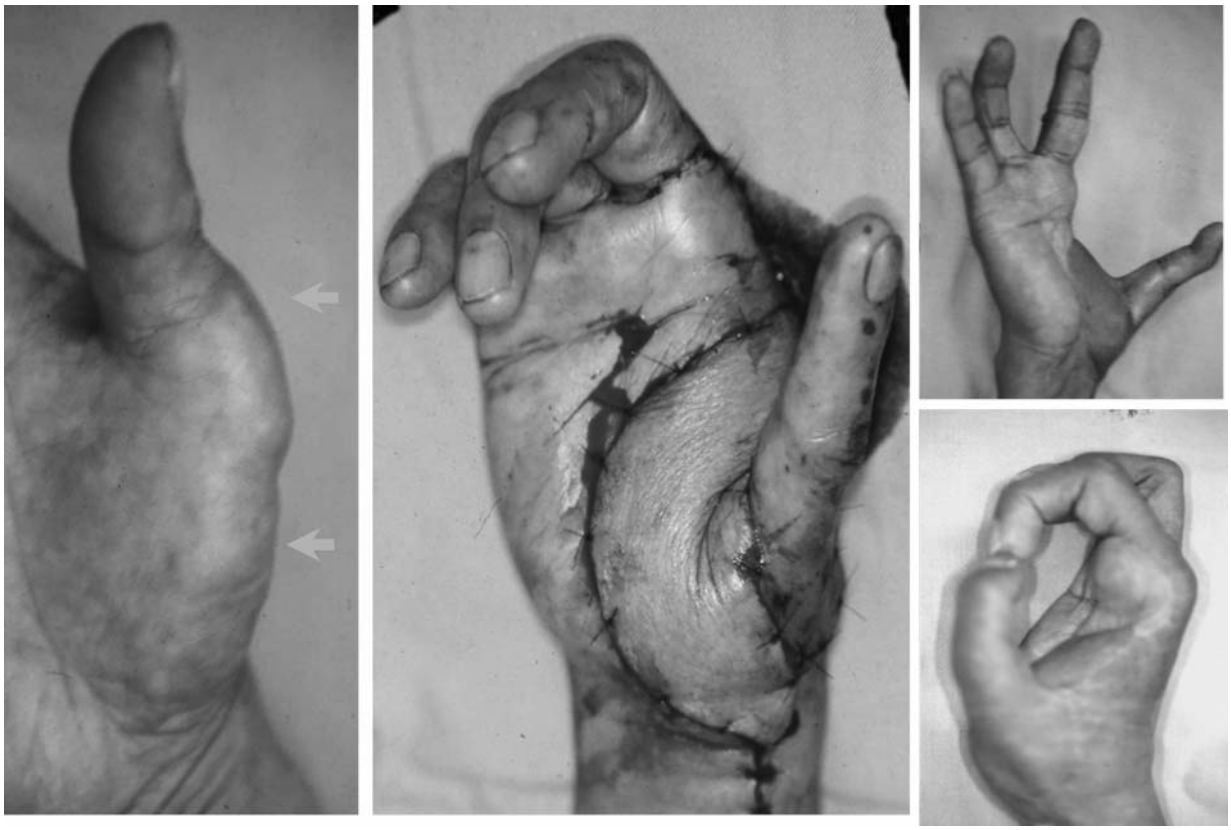

Figure 4. *A 61 year-old-man with synovial sarcoma in the thenar muscle was treated with wide resection, index finger transfer to the thumb and peroneal flap. Primary digital ray transposition is a good choice but index-to-thumb transfer frequently results in poor outcome due to emotional difficulty.*

Vascularized nerve grafting. The clinical application of vascularized nerve graft (VNG) has also so far been limited to trauma cases (38), with only a few studies focused on musculoskeletal oncology (39). Peripheral nerve defects have conventionally undergone reconstruction using non-vascularized nerve grafts which survive by revascularization from the surrounding tissue. VNGs offer two advantages. Firstly, they have an associated and hence immediate blood supply (40). By avoiding a period of revascularization, this can reduce intra-neural fibrosis secondary to ischemia. Secondly, continuous nutrition of the nerve may promote rapid axonal regeneration, thus reducing the time required for re-innervation of motor end plates and sensory end organs (41).

To our knowledge, Koshima *et al*. were the first to apply VNG for oncological reconstruction (39). They reported the case of a 28-year-old woman with a rhabdomyosarcoma originating in the biceps. Wide resection of the tumor resulted in a 12-cm length defect of the median nerve and brachial artery. A long vascularized femoral nerve graft based on the descending branch of the lateral circumflex femoral vessel was interposed into the median nerve gap. We have treated an interesting case with synovial sarcoma of the wrist. The 8-cm long ulnar nerve defect was reconstructed by vascularized, folded sural nerve graft with the peroneal flap. This patient had excellent nerve regeneration. Because of its low morbidity, we believe the most appropriate donor for VNG is the sural nerve. We suggest that nerve defects of more than 8 cm in length should be reconstructed using VNG.

Microsurgical reconstruction for massive osteochondral defects. The therapeutic goal of bone tumor reconstruction is a one-stage procedure that provides secure bony consolidation and allows for early physical therapy (42). Due to excellent adaptation, a free vascularized fibula graft is the best procedure for forearm bone reconstruction following tumor resection (43). For defects of the distal radius, other reconstructive procedures have been reported, including radial carpal joint reconstruction using fibula head, fibulo-scapho-lunate arthrodesis or total arthrodesis (44-51) (Figure 3). The fibular head transfer along with the shaft is an attractive method to replace the radio-carpal joint, but is technically demanding (50). Usui *et al*. reviewed six tumor patients with reconstruction using vascularized fibular head grafts (47). The postoperative complications were unexpectedly

high and included progressive degenerative changes, bony collapse due to poor vascularity of the fibular head, and volar subluxation resulting from incongruity between the fibular head and the proximal carpal row. This reconstruction should only be considered for patients engaged in light manual work.

If the carpal bones can be preserved, we first recommend fibulo-scapho-lunate arthrodesis using a vascularized fibular shaft graft, especially for young patients with high daily activity. Some wrist motion remains when the mid-carpal joint is preserved (52). This procedure involves a relatively simple technique to obtain good stability and reasonable mobility of the wrist. If the carpal bones cannot be preserved during tumor resection, total wrist fusion using a free vascularized fibula graft is indicated.

Reconstruction of the hand. Reconstruction after wide resection of digital malignant tumors remains a challenge. Small objects tend to fall from grasp through the space left by the missing digit. The adjacent fingers may scissor, further interfering with prehension and distorting the symmetry of the hand (53). For a single, central digit ray defect resulting from tumor resection, the technique of adjacent finger ray transposition such as index-to-middle or little-to-ring finger may be useful for closing the central gap between the remaining fingers (54). A total thumb defect from the base of the carpo-metacarpal joint can be reconstructed by index finger ray transposition (55, 56). Toe-to-thumb transfer or distraction lengthening is indicated for distal defects of the metacarpo-phalangeal joint (57, 58).

In our series, four patients underwent primary reconstruction with adjacent digital ray transposition. Functional results were good to fair in three patients with central ray amputation, but poor in one patient with total thumb resection (Figure 4). All patients experienced emotional difficulty with acceptance of a three-fingered hand. Careful preoperative informed consent may improve postoperative emotional outcomes.

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