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Functional Muscle Transfer after Oncologic Extremity Resection

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Abstract

Background Functional muscle transfer (FMT) can provide wound closure and restore adequate muscle function for patients with oncologic extremity defects. Herein we describe our institutional experience with FMT after oncological resection and provide a systematic review and meta-analysis of the available literature on this uncommon procedure.

Methods A single-institution retrospective review was performed, including all patients who received FMT after oncological resection from 2005 to 2021. For the systematic review and meta-analysis, PubMed, Cochrane, Medline, and Embase libraries were queried according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines; results were pooled, weighted by study size, and analyzed.

Results The meta-analysis consisted of seven studies with 70 patients overall, demonstrating a mean Medical Research Council (MRC) score of 3.78 (95% confidence interval: 2.97–4.56; $p < 0.01$). The systematic review included 28 studies with 103 patients. Receipt of adjuvant chemotherapy was associated with significantly lower mean MRC score (3.00 ± 1.35 vs. 3.90 ± 1.36; $p = 0.019$). Seventy-four percent of the patients underwent free FMT, with the most common donor muscle being the latissimus dorsi (55%). The flap loss rate was 0.8%. Neoadjuvant chemotherapy ($p = 0.03$), radiotherapy ($p = 0.05$), pedicled FMTs ($p = 0.01$), and a recipient femoral nerve ($p = 0.02$) were associated with significantly higher complication rates. The institutional retrospective review identified 13 patients who underwent FMT after oncological resection with a median follow-up time of 21 months (range: 6–74 months). The most common tumor necessitating FMT was undifferentiated pleomorphic sarcoma (77%), and the most common donor muscle was the latissimus dorsi (62%). A high body mass index was associated with prolonged neuromuscular recovery ($R = 0.87$, $p = 0.002$).

Conclusion FMT after oncological resection may contribute to improved extremity function. Careful consideration of risk factors and preoperative planning is imperative for successful FMT outcomes.

Keywords
- ► flaps
- ► surgical
- ► soft-tissue sarcoma
- ► functional muscle transfer

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Soft-tissue sarcoma (STS) is a rare mesenchymal tumor that accounts for less than 1% of all malignancies.[1] Historically, for extremity STS, amputation was the recommended surgical treatment.[2] Contemporary treatment of extremity STS centers on wide local excision of the tumor, with the goal of limb preservation. When combined with radiotherapy, limb-preserving surgery demonstrated 5-year survival rates comparable with those for amputation, solidifying limb preservation as the standard of care.[3] However, surgical resection with wide margins frequently results in loss of major musculotendinous and neurovascular structures, which can cause significant disability despite the fact that the limb has been "preserved." Functional muscle transfer (FMT) is one technique that can be used to reconstruct STS extirpations and may restore some degree of function to the limb.

FMT involves transferring a functioning donor muscle with a neurovascular pedicle to a new location to assume an independent function. FMT is indicated when a tumor resection eliminates the ability to move the extremity along one or more joints. For instance, an STS located in the anterior compartment of the leg would require an en bloc resection, which could eliminate the ability to dorsiflex the ankle; in this scenario, FMT could be used to not only close the wound and resurface the leg but also restore ankle dorsiflexion. FMT can be harvested with the muscle's neurovascular pedicle for a distant transfer or islandized on its neurovascular pedicle and rotated. The latissimus dorsi (LD),[4–7] gracilis,[8–10] tensor fasciae latae (TFL),[5,7,8,11] and vastus lateralis[12–15] are the most commonly used donor muscles for FMT. Aside from restoring motor function to the involved extremity, FMT with vascularized, nonirradiated tissue provides several other reconstructive advantages over local options, all of which potentiate more reliable wound healing: improved soft tissue resurfacing, ample tissue volume for filling dead space, and durable coverage or critical neurovascular structures and/or bone.[16–18]

Studies evaluating outcomes following FMT are heterogeneous, involving various techniques and metrics. To assess the feasibility, outcomes, and predictors of success or failure of FMT, a review of the literature is needed. Because our institution is a large international referral center, we have a unique perspective on the use of FMT for complex and uncommon oncological defects. In this study, we analyze oncological FMT using a two-pronged approach: (1) a systematic review and meta-analysis of the extant literature and (2) an in-depth analysis of our own institutional experience.

Methods

Systematic Review

Search Strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were used to develop the literature search protocol. PubMed, Cochrane Library, Medline, and Embase databases were searched by two independent reviewers in August 2021 using the following keywords: muscle OR flap OR free tissue flap AND transfer OR reconstruction AND soft tissue neoplasm OR sarcoma OR soft tissue cancer AND extremity OR limb OR shoulder OR arm OR hand OR finger OR digit OR thumb OR hip OR leg OR ankle OR foot OR toe (►**Fig. 1**).

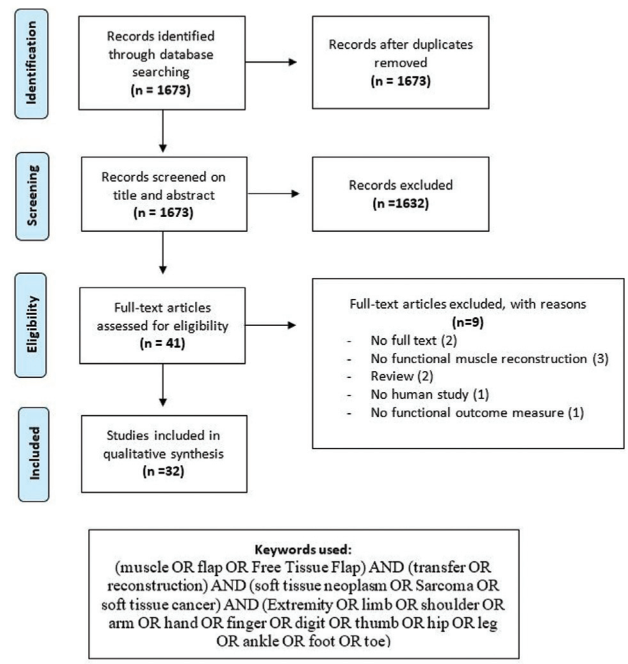

Fig. 1 Flow chart depicting the study selection for the systematic review.

Eligibility Criteria and Study Selection

Inclusion criteria included original English language articles reporting on FMT after oncological resection in humans from 1980 to 2021. Studies describing FMT for nononcological indications, studies with no individual patient data, systematic reviews, review articles, articles by the same author with identical data, meta-analyses, basic science studies, cadaver studies, editorials, and commentaries were excluded.

Data Extraction Process

The following data were extracted from the articles: study design, number of patients, patient characteristics, comorbidities, tumor characteristics, surgical techniques, complications, and functional outcomes. The quality of each study was evaluated using the parameters established by the Oxford Centre for Evidence-Based Medicine (OCEBM).

Methodological Assessment and Risk of Bias

The methodological quality and risk of bias of nonrandomized studies in meta-analyses were assessed using the Newcastle–Ottawa Scale.[19,20] A modified Newcastle–Ottawa Scale of six points was used to evaluate studies based on the following parameters: duration of follow-up, adequacy of follow-up, ascertainment of exposure to the intervention, representation of the exposed group, outcome not present at the start of the analysis, and outcome assessment.[19,21–23]

Case Series

We conducted a comprehensive review of all patients who underwent FMT after oncological resection at the University of Texas MD Anderson Cancer Center from March 2005 to June 2021. We collected patient demographics and comorbidities, tumor characteristics, surgical techniques, complications, and final extremity motor function status. Complications included seroma or hematoma requiring drainage, wound dehiscence, infection requiring antibiotics, total or partial flap loss, microvascular thrombosis, and any complication necessitating return to the operating room. Functional recovery was assessed using Medical Research Council (MRC) motor strength scores, time to initial neuromuscular recovery, and time to maximal neuromuscular recovery.

Statistical Analysis

RStudio software was used for statistical analyses. The Pearson chi-square test and Mann–Whitney U-test were used to assess associations between categorical variables. Analysis of variance and the Kruskal–Wallis test were used to compare continuous variables. Cumulative survival probabilities after FMT were estimated using the Kaplan–Meier product-limit method. *p*-Values less than 0.05 were considered significant.

Studies presenting individual patient data were assessed using the Newcastle–Ottawa Scale for inclusion in the meta-analysis. A meta-analysis with an accompanying forest plot was performed. Cochrane's Q and I^2 were used to assess heterogeneity among studies, with an I^2 less than 50% defined as low heterogeneity, 50 to 75% as moderate heterogeneity, and greater than 75% as high heterogeneity. A random-effects model was used to account for variation in studies.

Results

Systematic Review

Search Results

The search identified 1,673 articles (►**Fig. 1**). After employing our exclusion criteria, 28 articles—representing 103 patients—were appropriate for inclusion in the systematic review (►**Table 1**). The included articles were published from 1993 to 2021 and were categorized as level 4 or 5 according to OCEBM.[4–15,24–43]

Patient Demographics

The median patient age was 54 years (range: 6 months to 83 years). Forty-seven percent received preoperative radiotherapy, and 27% received preoperative chemotherapy. Fourteen percent and 11% received postoperative chemotherapy and postoperative radiotherapy, respectively. The median follow-up time was 23 months (range: 6–150 months), the median MRC score was 4 (range: 0–5), and the median time to first neuromuscular recovery was 4 months (range: 2–12 months). Pearson correlation testing demonstrated a weak positive correlation between age and MRC score ($R = 0.16$, $n = 82$, $p = 0.31$) (►**Supplementary Fig. S1**, available in the online version). Receipt of postoperative chemotherapy was associated with a significantly lower mean MRC score (3.0 ± 1.35 vs. 3.90 ± 1.36; $p = 0.019$).

Tumor Characteristics

Pleomorphic sarcoma was the most common tumor (29%), followed by liposarcoma (26%). Sixty-eight percent of the tumors involved the lower extremity. The thigh (57%) was the most commonly affected location, followed by the arm (17%). ►**Supplementary Fig. S2** (available in the online version) shows a histogram of the mean MRC scores by tumor type. We found no significant differences between tumor types and MRC scores ($p = 0.17$). There was also no significant difference in the time to first neuromuscular recovery by defect location (►**Supplementary Fig. S3**, available in the online version).

Flap Characteristics

Seventy-four percent of the patients received a free FMT. The most common donor muscle was the LD (55%), followed by the rectus abdominis (15%) and gracilis (13%). The femoral nerve was the most common recipient nerve (54%), followed by the sciatic (9%) and peroneal (9%) nerves. We found no significant differences in MRC score according to flap type ($p = 0.32$), donor muscle ($p = 0.16$), or recipient nerve ($p = 0.09$) (►**Supplementary Figs. S4** and **S5**, available in the online version). We also found no significant differences in time to first neuromuscular recovery according to flap type ($p = 0.43$), donor muscle ($p = 0.32$), or recipient nerve ($p = 0.22$) (►**Supplementary Figs. S6** and **S7**, available in the online version).

Complications

Eleven percent of the patients experienced complications (►**Table 2**). Pedicled FMT and receipt of preoperative chemotherapy or radiotherapy were associated with an increased risk of donor-site complications ($p = 0.01$, $p = 0.03$, and $p = 0.05$, respectively). Also, a recipient femoral nerve was associated with an increased risk of recipient-site complications ($p = 0.02$).

Comparison of Upper versus Lower Extremity FMT

Sixty-eight percent ($n = 70$) of patients had FMT for a lower extremity defect, while 32% had FMT for an upper extremity defect (►**Table 3**). Lower extremity FMT patients were more likely to receive preoperative radiotherapy (57.1 vs. 24.2%, $p = 0.003$) and free flaps (94.8 vs. 37.5%, $p = 0.001$) than upper extremity FMT patients. When compared with patients with lower extremity FMT, patients with upper extremity FMT were more likely to undergo reconstruction with LD (63.6 vs. 52.9%, $p = 0.037$), gracilis (15.2 vs. 11.4%, $p = 0.037$), but not rectus abdominis (0 vs. 21.4%, $p = 0.037$). In the upper extremity FMT group, there was a trend toward more donor-site (6.1 vs. 1.4%, $p = 0.239$) and recipient-site (12.1 vs. 7.1%, $p = 0.462$) complications, but the difference was not statistically significant. We found no difference in median [interquartile range, IQR] MRC score (4 [3–5] vs. 4 [3–5], $p = 0.956$) between lower and upper extremity FMT, but we observed longer time to median [IQR] first neuromuscular recovery in the lower FMT group (4.5 [4.0–4.75] vs. 3.0 [2.25–5.25], $p = 0.956$), albeit not statistically significant.

Table 1 Study characteristics

Study	No. of patients	Mean age, y	Neoadjuvant therapy (%)	Adjuvant therapy (%)	Tumor type (%)	Body location (upper or lower)	Tumor location	Type of flap (pedicled or free flap)	Donor muscle	Recipient nerve	Donor-site complication	Recipient-site complication	MRC	Time to first neuromuscular function (mo)	Time to maximal neuromuscular function (mo)	Follow-up time (mo)
Barrera-Ochoa 2017	1	43	Chemotherapy (100%)	Radiotherapy (100%)	Synovial sarcoma (100%)	Lower	Hip abductors	Free flap	Latissimus dorsi	Superior gluteal nerve			5	2	4	
Beltrami 2018	2	26.5	Chemotherapy (50%)	Chemotherapy (50%)	Ewing sarcoma (50%), synovial sarcoma (50%)	Upper	Scapular region	Pedicled	Latissimus dorsi				2.5			18
Dillon 2015	1	73	Radiotherapy (100%)	NA	Myxoid liposarcoma (100%)	Lower	Antero-lateral thigh	Free flap	Vastus lateralis, tensor fasciae latae	Posterior division of femoral nerve						
Doi 1998	2	25.5	NA	NA	Synovial sarcoma (100%)	Upper (50%), lower (50%)	Dorsal forearm (50%), tibialis anterior (50%)	Free flap	Gracilis	Posterior interosseous nerve, tibialis anterior				4		
Doi1999	17	42.8	Chemotherapy (53%)	Chemotherapy (53%)	Liposarcoma (47%), synovial sarcoma (18%), fibrous histiocytoma (12%), leiomyosarcoma (6%), schwannoma (6%), myxoid chondrosarcoma (6%), fibrosarcoma (6%)	Lower (88%), upper (12%)	Thigh (65%), popliteal (12%), anterior lower leg (12%), dorsal forearm (6%), shoulder (6%)	Free flap	Latissimus dorsi (71%), fracilis (18%), tensor fasciae latae (6%), rectus femoris (6%)	Femoral (41%), sciatic (35%), deep peroneal (12%), radial (6%), axial (1%)		Skin necrosis of skin graft (6%)	2.3	5.3		60.8
Doi 1993	15	44	Chemotherapy (80%)	Chemotherapy (60%)	Liposarcoma (40%), fibrous histiocytoma (20%), chondrosarcoma (20%), leiomyosarcoma (13%), schwannoma (7%)	Lower (93%), upper (7%)	Thigh (93%), forearm (7%)	Free flap	Latissimus dorsi (93%), gracilis (7%)				3.4	7.7		26.8
Garcia 2021	1	76	Chemotherapy (100%)	Radiotherapy (100%)	Pleiomorphic sarcoma (100%)	Upper	Anterior arm	Pedicled	Latissimus dorsi	Musculocutaneous nerve			4			
Goertz 2009	1	2.75	NA	NA	Papillary intralymphatic angioendothelioma (100%)	Lower	Dorsal lower thigh	Free flap	Latissimus dorsi	Tibial nerve						
Grinsell 2012	20		Radiotherapy (100%)	NA	Pleiomorphic sarcoma (60%), liposarcoma (15%), dermatofibrosarcoma protuberans (5%), chondroblastic osteosarcoma (5%), neurofibrosarcoma (5%), angiosarcoma (5%), fibrosarcoma (5%)	Lower (85%), upper (15%)	Thigh (60%), leg (20%), hip extensor (10%), arm (10%), scapular region (10%)		Latissimus dorsi (45%), gracilis (35%), transverse rectus abdominis (15%), rectus abdominis (5%)			Flap failure (5%)	4.4			

Table 1 (*Continued*)

Study	No. of patients	Mean age, y	Neoadjuvant therapy (%)	Adjuvant therapy (%)	Tumor type (%)	Body location (upper or lower)	Tumor location	Type of flap (pedicled or free flap)	Donor muscle	Recipient nerve	Donor-site complication	Recipient-site complication	MRC	Time to first neuromuscular function (mo)	Time to maximal neuromuscular function (mo)	Follow-up time (mo)
Grinsell 2019	11	63.8	Radiotherapy (100%)	NA	Pleomorphic sarcoma (100%)	Lower (100%)	NA	Free flap (73%), pedicle (27%)	Rectus abdominis	Femoral			4.2			19.8
Hasmat 2019	27	72	NA	NA	Squamous cell carcinoma (63%)	Upper	Face	Free flap	Vastus lateralis							18.7
Hattori 2001	1	20	NA	NA	Soft tissue sarcoma	Upper	Finger	Free flap	Gracilis				4	2		16
Huayllani 2020	1	71	Radiotherapy (100%)	NA	Pleomorphic sarcoma (100%)	Lower	Anterior thigh	Free flap	Latissimus dorsi	Motor branch of femoral						
Ihara 1997	1	60	NA	NA	Liposarcoma (100%)	Upper	Deltoid region	Free flap	Tensor fasciae latae	Motor branch of axillary nerve				3	24	36
Ihara 2000 Successful	1	27	Chemotherapy (100%)	Chemotherapy (100%)	Synovial sarcoma (100%)	Upper	Right shoulder	Pedicled	Latissimus dorsi					6		
Ihara 2000	1	62	NA	NA	Myxoid chondrosarcoma (100%)	Lower	Gluteal region	Free flap	Latissimus dorsi	Superior gluteal nerve						
Ihara 1999	23	44	Chemotherapy (57%)	Chemotherapy (43%)	Liposarcoma (43%), synovial sarcoma (13%), malignant fibrous histiocytoma (13%), chondrosarcoma (13%), leiomyosarcoma (9%), malignant schwannoma (4%), fibrosarcoma (4%)	Lower (91%), upper (9%)	Posterior thigh(43%), anterior thigh (35%), anterior lower leg(9%), dorsal forearm (4%), shoulder (4%), buttock (4%)	Free flap	Latissimus dorsi (78%), gracilis (13%), tensor fasciae latae (4%), rectus femoris (4%)	Motor branch of sciatic nerve (43%), femoral nerve (35%), posterior interosseous nerve (4%), axillary nerve (4%), superior gluteal nerve (4%)		Venous thrombosis of flap (9%), skin flap necrosis (4%)	3.6	1.5		60
Ihara 2003	5	43	Chemotherapy (40%)	Chemotherapy (40%)	Liposarcoma (20%), dermatofibrosarcoma (20%), liposarcoma (20%), synovial sarcoma (20%), osteosarcoma (20%)	Upper	Trapezius (60%), deltoid region (40%)	Pedicle (60%), Free flap (40%)	Latissimus dorsi (60%), tensor fasciae latae (40%)				4.4	3		81.8
Innocenti 2009	11	45.5	Chemotherapy (64%); radiotherapy (73%)	NA	Liposarcoma (45%), fibrosarcoma (36%), pleiomorphic sarcoma (9%), osteosarcoma (9%)	Lower	Anterior thigh (100%)	Free flap	Latissimus dorsi	Motor branch of femoral nerve		Infection (4%)		8.3		

(*Continued*)

Table 1 (*Continued*)

Study	No. of patients	Mean age, y	Neoadjuvant therapy (%)	Adjuvant therapy (%)	Tumor type (%)	Body location (upper or lower)	Tumor location	Type of flap (pedicled or free flap)	Donor muscle	Recipient nerve	Donor-site complication	Recipient-site complication	MRC	Time to first neuromuscular function (mo)	Time to maximal neuromuscular function (mo)	Follow-up time (mo)
MacArthur 2019	3	53[a]	Chemotherapy (22%)[a]; radiotherapy (78%)[a]	NA	Pleiomorphic sarcoma (35%)[a], myxofibrosarcoma (26%)[a], leiomyosarcoma (17%)[a], liposarcoma (4%)[a], extraosseous osteosarcoma (4%)[a], synovial sarcoma (4%)[a], epithelioid sarcoma (4%)[a], dermatofibrosarcoma protuberans (4%)[a]		Knee		Gracilis							14[a]
Moschella 2010	1	72	NA	NA	Liposarcoma (100%)	Lower	Posterior tibial	Free flap	Rectus femoris	Motor branch of gastrocnemius			3	3		
Mundinger 2014	7	54	Radiation (71%)	Radiation (29%)	Fibrous histiocytoma (43%), pleomorphic sarcoma (43%), synovial cell sarcoma (14%)	Upper (100%)	Biceps (86%), triceps (14%)	86% Pedicle, 14% Free	Latissimus dorsi (86%), gracilis (14%)		Seroma (14%), chronic pain (14%)	Cellulitis (14%), partial flap loss (14%), arterial thrombosis (14%)				43.3[a]
Muramatsu 2010	59	51.6	NA	Radiation therapy	Fibrous histiocytoma (49%), liposarcoma (15%), synovial sarcoma (8%), chondrosarcoma (8%), malignant peripheral nerve sheath tumor (7%), leiomyosarcoma (7%), osteosarcoma (5%), Ewing sarcoma (3%), rhabdomyosarcoma (2%), epithelioid sarcoma (2%), fibrosarcoma (2%)	Lower (41%), upper (15%), trunk (44%)		Free flap (54%), Pedicle (47%)	Latissimus dorsi (56%), tensor fasciae latae (17%), rectus abdominis (7%), gracilis (3%)			Seroma (5%), partial necrosis (2%)		5.7		50.2
Muramatsu 2014	4	68	Chemotherapy (25%)	NA	Liposarcoma (50%), pleomorphic sarcoma (50%)	Upper (100%)	Deltoid region	Pedicled	Latissimus dorsi	Thoracodorsal nerve						
Nascimento 2019	1	81	NA		Spindle cell tumor	Upper	Biceps	Pedicled	Latissimus dorsi							12
Nicoli 2016	1	33	NA	Radiotherapy (100%)	Liposarcoma (100%)	Upper	Arm	Pedicled	Latissimus dorsi	Pronator teres motor branch			4			12
Ozols 2020	1	0.5	Chemotherapy (100%)	Chemotherapy (100%)	Rhabdomyosarcoma (100%)	Lower	Posterior lower limb	Free flap	Vastus lateralis	Gastrocnemius muscular nerves (tibial nerve)			4			24

Table 1 (*Continued*)

Study	No. of patients	Mean age, y	Neoadjuvant therapy (%)	Adjuvant therapy (%)	Tumor type (%)	Body location (upper or lower)	Tumor location	Type of flap (pedicled or free flap)	Donor muscle	Recipient nerve	Donor-site complication	Recipient-site complication	MRC	Time to first neuromuscular function (mo)	Time to maximal neuromuscular function (mo)	Follow-up time (mo)
Pritsch 2007	15	45	Chemotherapy (53%)	Radiotherapy (87%); chemotherapy (60%)	Fibrous histiocytoma (27%), high-grade liposarcoma (20%), low-grade liposarcoma (7%), leiomyosarcoma (20%), MPNST (13%), fibromatosis (13%)	Lower	Anterior thigh	Pedicled	Sartorius, biceps femoris, semitendinosus		Wound dehiscence (2%)		4.33			78
Schoeller 2002	1	9	Chemotherapy (100%)	Radiotherapy (100%); chemotherapy (100%)	Ewing sarcoma (100%)	Upper	Arm	Free flap	Flexor hallucis	Musculocutaneous nerve						
Stranix 2018	4	56.3	Chemotherapy (75%)	Radiotherapy (50%)	Spindle cell tumor (50%), myxofibrosarcoma (25%), liposarcoma (25%)	Lower (75%), upper (25%)	Anterior leg (50%), anterior thigh (25%), dorsal forearm (25%)	Free flap	Tensor fasciae latae with vastus lateralis (75%), tensor fasciae latae with IT band (25%)	Deep peroneal nerve (75%), posterior interosseous nerve (25%)				6		25
Walley 2017	3	53.7	Radiotherapy (66%); chemotherapy (33%)	NA	Osteosarcoma (33%), liposarcoma (33%), myxofibrosarcoma (33%)	Lower	Anterior thigh (66%), distal femur (33%)	Free flap	Vastus lateralis	Femoral nerve			4.33		5.5	
Willcox 2003	1	21	Chemotherapy (100%)	NA	Osteosarcoma (100%)	Lower	Thigh	Free flap	Latissimus dorsi	Femoral nerve						36

Abbreviations: MPNST, malignant peripheral nerve sheath tumor; MRC, Medical Research Council.
[a]data reported from this study included non-FMT patients.

Table 2 Surgical complications identified in the systematic review

Surgical complications	No. of patients (%)
Total	11 (100)
Donor-site complications	
Seroma	1 (9)
Cellulitis	1 (9)
Chronic pain	1 (9)
Recipient-site complications	
Infection	2 (18)
Flap failure	2 (18)
Arterial thrombosis	1 (9)
Necrosis	1 (9)
Wound breakdown	1 (9)
Epidermolysis	1 (9)

Meta-Analysis

The meta-analysis consisted of seven studies, representing the pooled outcomes of 70 patients. The mean modified Newcastle–Ottawa Scale score for these studies was 6/6.[7,10,24,25,37–39] Because the I^2 statistic indicated inter-study heterogeneity ($I^2 = 89\%$), we used a random-effects model to mitigate data heterogeneity. This analysis identified a mean MRC score of 3.78 (95% CI: 2.9–4.6; $p < 0.01$), indicating that most patients' FMTs provided the motor force necessary to overcome gravity at the affected joint (►**Fig. 2**).

Case Series

Patient and Tumor Characteristics

Our chart review identified 13 patients who underwent FMT after oncological resection with a median age of 57 years (IQR: 14–77 years), median body mass index (BMI) of 27 kg/m^2 (IQR: 20–48 kg/m^2), and median follow-up time of 21 months (IQR: 6–74 months). The reconstructions were performed by a total of eight plastic surgeons from 2005 to

Table 3 Comparative analysis of lower and upper extremity FMT in the systematic review

	Tumor location		
Variable	Lower extremity	Upper extremity	p-Value
Number of patients, *n* (%)	70 (68.0)	33 (32.0)	
Age, median (IQR)	54 (34–63)	54 (27–71)	0.946
Follow-up, median (IQR)	24 (14–52)	21 (15–56)	0.781
Preoperative chemotherapy, *n* (%)	21 (30.0)	28 (21.2)	0.477
Preoperative radiotherapy, *n* (%)	40 (57.1)	8 (24.2)	**0.003**
Tumor type, *n* (%)			0.170
Pleomorphic sarcoma	24 (34.3)	6 (18.2)	
Liposarcoma	18 (25.7)	8 (24.2)	
Others	28 (40.0)	19 (57.6)	
Flap type, *n* (%)			<**0.001**
Free flap	55 (94.8)	12 (37.5)	
Pedicled flap	3 (5.2)	20 (62.5)	
Donor muscle, *n* (%)			**0.037**
Latissimus dorsi	37 (52.9)	21 (63.6)	
Rectus abdominis	15 (21.4)	0 (0)	
Gracilis	8 (11.4)	5 (15.2)	
Others	10 (14.3)	7 (21.2)	
Any complication, *n* (%)	6 (8.6)	5 (15.1)	0.323
Recipient-site complication, *n* (%)	5 (7.1)	4 (12.1)	0.462
Donor-site complication, *n* (%)	1 (1.4)	2 (6.1)	0.239
MRC, median (IQR)	4 (3–5)	4 (3–5)	0.956
First neuromuscular recovery, mo, median (IQR)[a]	4.5 (4.0–4.75)	3.0 (2.25–5.25)	0.085

Abbreviations: FMT, functional muscle transfer; IQR, interquartile range; MRC, Medical Research Council.
Note: Statistically significant *p*-values are indicated in bold.
[a]Only one patient with known tumor location reported maximal neuromuscular recovery.

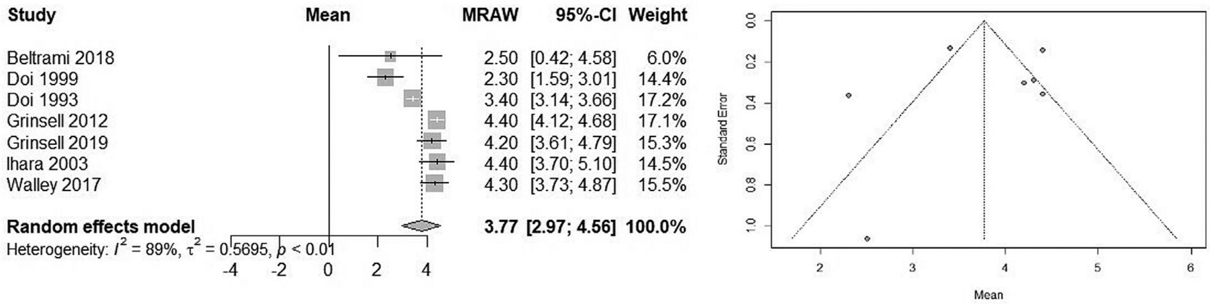

Fig. 2 Forest plot of mean MRC scores (*left*) and funnel plot of the studies included in the meta-analysis ($n = 7$). MRC, Medical Research Council.

2021. Seventy-seven percent ($n = 10$) of the patients received preoperative chemotherapy (►**Table 4**). The triceps was the most commonly affected muscle group (38%), followed by the biceps, quadriceps, and anterior compartment of the leg (all 15%) (►**Table 5**).

Oncologic Outcomes

The most common tumor (77%) was undifferentiated pleomorphic sarcoma, followed by liposarcoma (15%) and osteosarcoma (8%). Sixty-two percent of the tumors ($n = 8$) were located in the upper extremity. The arm was the most commonly affected location (62%), followed by the thigh (23%). At the time of the final follow-up, 43% ($n = 6$) of patients were alive. The median duration of follow-up for surviving patients was 31.50 months (IQR: 18.0–46.50 months). During the follow-up period, 31% of patients ($n = 4$) developed a local tumor recurrence, and 85% developed tumor metastasis. ►**Fig. 3** depicts a Kaplan–Meier curve for the probability of survival following FMT. The 1-year and 3-year survival probabilities after FMT were estimated to be 84.6 and 76.1%, respectively.

Table 4 Patient demographics from the institutional case series

Characteristic	No. of patients (%)
Median age, y (IQR)	57 (47–70)
Sex	
Female	5 (38)
Male	8 (62)
Median BMI, kg/m^2 (IQR)	27 (25–32)
Tobacco use	1 (8)
Comorbidities	
Coronary artery disease	1 (8)
Diabetes mellitus	2 (15)
Hypertension	7 (54)
Pulmonary disease	1 (8)
Renal disease	1 (8)
Preoperative radiotherapy	9 (69)
Postoperative radiotherapy	3 (23)
Preoperative chemotherapy	10 (77)
Postoperative chemotherapy	9 (69)
Median follow-up time, mo, median (IQR)	21.1 (6–47)

Abbreviations: BMI, body mass index; IQR, interquartile range.

Flap Characteristics

Among the 13 patients in the chart review, 7 received a free FMT, whereas 8 received a pedicled FMT. Eleven flaps were musculocutaneous, whereas 2 were buried muscle-only flaps. The LD flap was the most common flap (62%), followed by the gracilis (23%) and vastus lateralis (15%) flaps. ►**Figs. 4** to **6** and ►**Videos 1** to **3** depict representative case examples of these reconstructions.

Video 1

Video of functional recovery 17 months postoperatively of the patient depicted in ►**Fig. 3**. The patient underwent functional muscle transfer with a pedicled latissimus dorsi myocutaneous flap for reconstruction of the arm. The patient achieved maximal neuromuscular function, with an MRC score of 5. The patient was able to extend her arm against resistance despite the complete absence of her triceps muscle. MRC, Medical Research Council. Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/html/10.1055/a-1887-7530.

Video 2

Intraoperative video of the patient depicted in ►**Fig. 6**. The patient underwent functional muscle transfer using a free latissimus dorsi myocutaneous flap for reconstruction of the thigh. After neural coaptation, stimulation of the recipient motor nerve at 2 mA produced contraction across the anastomosis in the latissimus dorsi muscle. MRC, Medical Research Council. Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/html/10.1055/a-1887-7530.

Video 3

Video of functional recovery 13 months postoperatively of the patient depicted in ►**Fig. 6**. The patient underwent functional muscle transfer using free latissimus dorsi myocutaneous flap for reconstruction of the thigh. The video shows an unassisted extension of the left knee against gravity. Upon physical examination, his MRC score was 5. He reported being able to mountain bike and jog. MRC, Medical Research Council. Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/html/10.1055/a-1887-7530.

Functional Outcomes

One patient required a reoperation due to a complication; there were no flap losses (►**Table 6**). The median MRC score was 5 (range: 2–5). Among the recipient nerves, the deep peroneal nerve had the lowest median MRC score (2.25 [range: 2–2.5]), whereas the femoral nerve, nerve to triceps, and vastus lateralis had a median MRC score of 5 (range: 5–5). Gracilis FMTs had a lower median MRC score (2.5) than did LD (5) and vastus medialis (5) FMTs.

The median time to first neuromuscular recovery and maximal neuromuscular recovery was 1.5 months (range: 0.3–6.4 months) and 7.6 months (range: 2.3–23.8 months), respectively. A high BMI was associated with delayed first neuromuscular recovery ($R = 0.87$, $p = 0.002$) (►**Supplementary Fig. S8**, available in the online version).

Discussion

Pedicled or free FMT can be used to provide wound closure and improve motor function after resection of a connective tissue malignancy, particularly when a substantial amount of muscle and skin is resected. In our systematic review, we identified 28 studies, representing 103 patients who underwent FMT after oncological resection. The meta-analysis results demonstrated a mean MRC score of 3.78 (95% CI: 2.97–4.56), indicating functional outcomes consistent with the ability of the reconstructed extremity to counteract the force of gravity. In addition, receipt of adjuvant chemotherapy was associated with markedly lower MRC scores. We identified a complication rate of 11%, with only two patients experiencing flap loss. The variables associated with increased risk of complications were neoadjuvant chemotherapy and radiotherapy, pedicled flaps, and a recipient femoral nerve. Our institutional chart review identified similar patient characteristics and functional outcomes to those found in the systematic review. In addition, our chart review identified that greater BMI was significantly associated with delayed neuromuscular recovery. Taken together, the results of the systematic review and our institutional chart

Table 5 Surgical characteristics of the institutional case series

Characteristic	No. of patients (%)
Type of tumor	
Undifferentiated pleomorphic sarcoma	10 (77)
Liposarcoma	2 (15)
Osteosarcoma	1 (8)
Tumor location	
Arm	8 (62)
Thigh	3 (23)
Leg	1 (8)
Thigh and leg	1 (8)
Muscle group reconstructed	
Triceps	5 (38)
Biceps	2 (15)
Quadriceps	2 (15)
Anterior compartment, leg	2 (15)
Posterior compartment, thigh	1 (8)
Rotator cuff	1 (8)
Type of FMT	
Pedicled	6 (46)
Free flap	7 (54)
Type of flap	
Musculocutaneous	11 (85)
Buried	2 (15)
Donor muscle	
LD	8 (62)
Gracilis	3 (23)
Vastus lateralis	2 (15)
Recipient vessels	
Tibial	2 (15)
Brachial	1 (8)
Profunda brachii	1 (8)
Superficial femoral artery	1 (8)
Descending femoral circumflex	1 (8)
Lateral femoral circumflex	1 (8)
Adjuvant techniques	
Tenodesis	4 (31)
Tendon transfer	4 (31)
Nerve coaptation	8 (62)
Nerve graft	1 (8)
Median size of harvested muscle, cm^2 (IQR)	95 (60–120)

Abbreviations: FMT, functional muscle transfer; IQR, interquartile range; LD, latissimus dorsi.

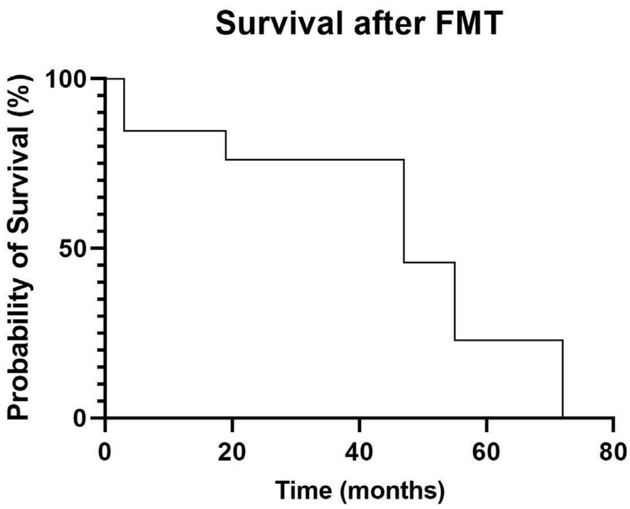

Fig. 3 Kaplan–Meier Curve for survival probability after FMT in the institutional case series. FMT, functional muscle transfer.

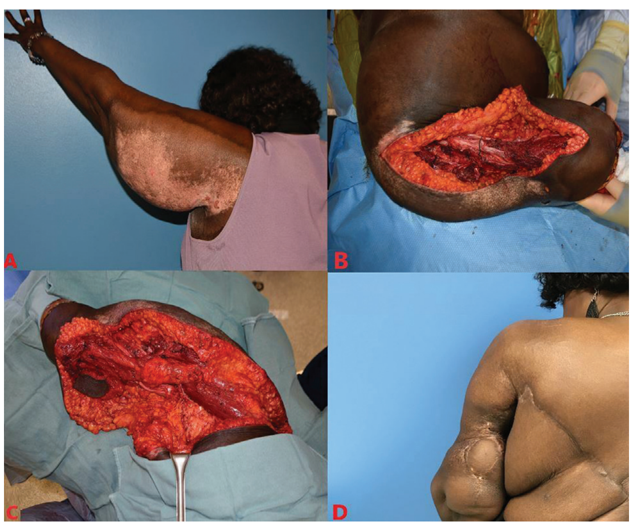

Fig. 4 Case example of FMT for reconstruction of the arm. **(A)** A large dedifferentiated liposarcoma involving the left posterior arm in a 71-year-old woman. **(B)** The resection defect after tumor removal. The elbow is on the right side of the image, and the axilla is on the left. The entire triceps muscle was removed, but the radial nerve was spared. **(C)** The ipsilateral LD muscle was rotated as a pedicled myocutaneous flap. The proximal LD was inset to the proximal posterior humerus with a series of bone-anchored sutures. The distal LD was secured to the remnant triceps tendon at the olecranon with a modified, layered Krakow repair. **(D)** Image obtained 15 months after the procedure showing that the wound healed with no evidence of disease. The flap's skin paddle is visible along the distal posterior arm. FMT, functional muscle transfer; LD, latissimus dorsi.

review suggest that FMT is an effective technique for improving extremity motor function after oncological resection.

Studies have identified several qualities of an appropriate donor muscle[44,45]: (1) adequate power and excursion, (2) expendable and adaptable muscle type, (3) sufficient range of motion, and (4) minimal functional impairment after harvesting. Considering these criteria, the LD, vastus lateralis, gracilis, TFL, rectus femoris, and rectus abdominis are each considered appropriate donor muscles for FMT. In our systematic review, the LD was the most commonly used donor muscle, employed in more than half of reported cases to reconstruct defects in the anterior[10,33,35,41,43] and posterior[33] arm, deltoid,[7,34] shoulder,[4,7] and scapular region.[38] Terzis and Kostopoulos[46] reported that the LD achieved greater muscle power than did the rectus femoris and gracilis. Our systematic review found that most authors reported that the rectus abdominis and vastus lateralis achieved greater muscle power (mean MRC score: 4.3) than did the TFL (mean MRC score: 4), LD (mean MRC score: 3.5), gracilis (mean MRC score: 3.1), and rectus femoris (mean MRC score: 3). Our case series corroborated the findings of the systematic review, with the gracilis muscle having a lower median MRC score (2.5) than that of the LD (5) and vastus lateralis (5) FMTs. With its lower power, gracilis FMT is better suited for oncological reconstruction in the forearm, where less excursion and force are needed. Doi et al[25] reported three cases of oncological reconstruction for extensive finger flexor and extensor defects. Two patients received a gracilis flap, whereas the third received an LD flap. The gracilis FMT patients had good outcomes, with MRC scores of 3, whereas the patient with the LD had poor flexor muscle balance because the LD was too powerful in relation to the native forearm extensors. Therefore, donor muscle selection requires careful consideration of the defect characteristics, most importantly, the required muscle excursion and force needed for the anatomic area in question.

Although the rate of complications in our institutional review was higher than that reported in the literature (54 vs. 11%, respectively), the majority of cases (86%) were minor complications that did not necessitate a return to the operating room. In addition, no patient experienced flap loss, compared with two in the systematic review. Despite this, the higher incidence of complications in our institutional series could be attributed to the complexity of the cases and the longer follow-up period. Patients in the institutional review received more chemotherapy (77 vs. 27%) and radiotherapy (69 vs. 47%), and had a higher proportion of pedicled flaps (46 vs. 26%), all of which are associated with a higher risk of complications.

The time required to achieve neuromuscular recovery after FMT varies depending on patient characteristics, the donor muscle, and the recipient nerve. In our retrospective review, we found that patients with high BMIs are likely to experience delayed neuromuscular recovery. In our systematic review, use of the TFL as the donor muscle had the longest mean time to first neuromuscular recovery (5.2 months), followed by the LD (4.9 months), gracilis (3.7 months), and rectus femoris (3.5). Authors in only two studies reported the time to maximal neuromuscular recovery. Barrera-Ochoa et al[36] reported that this time was 4 months for a free LD flap after excision of a synovial sarcoma in the hip, with an MRC score of 5. In comparison, Ihara et al[11] reported that the time to maximal neuromuscular recovery was 24 months for a free TFL flap after excision of a liposarcoma in the deltoid, also with an MRC score of 5. In our case series, a vastus lateralis FMT was

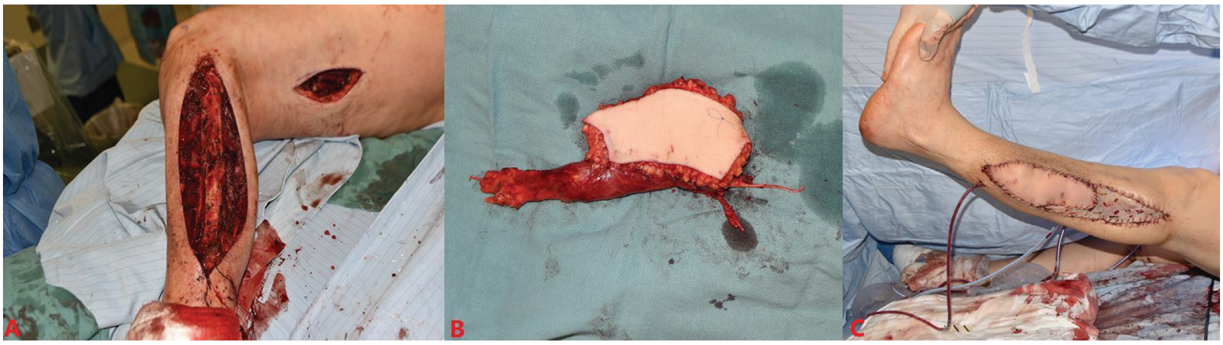

Fig. 5 Case example of FMT for reconstruction of the leg. **(A)** A 68-year-old woman presented with recurrent pleomorphic sarcoma involving the lateral and anterior compartments of the left leg. **(B)** A right free gracilis myocutaneous flap including the obturator nerve to the muscle that was harvested from the patient. **(C)** The gracilis muscle was revascularized to the anterior tibial artery in an end-to-side format, and the paired venae comitantes were end to end. The flap's obturator nerve was coapted to the common peroneal nerve end to end with epineurial sutures. The muscle was appropriately tensioned and inset. The distal gracilis tendon was inset to the anterior tibialis and peroneus longus muscle stumps using a modified Pulvertaft weave technique. The proximal gracilis muscle belly was inset to the lateral knee joint capsule. Finally, a pedicled lateral gastrocnemius muscle flap and skin graft were required for complete closure of the defect. FMT, functional muscle transfer.

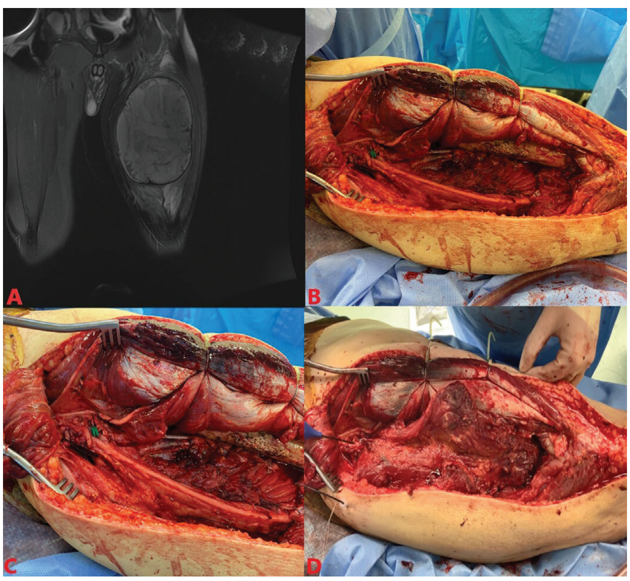

Fig. 6 Case example of FMT for reconstruction of the thigh. **(A)** Preoperative magnetic resonance image of an 11 × 14 × 18 cm tumor obliterating the quadriceps compartment. **(B)** Resection of the tumor included the entirety of the adductor compartment, vastus medialis, and vastus intermedius. The rectus femoris and vastus lateralis were rendered ischemic and congested by the vascular resection. The femur was exposed without periosteum. **(C)** The LD was harvested as a myocutaneous flap. The skin paddle was de-epithelialized and placed adjacent to the femur "upside down" to decrease adhesions to the femur and increase excursion. **(D)** The LD flap was anastomosed to the vascular stumps of the descending branch of the lateral femoral circumflex artery and vein, which had been ligated during resection. The thoracodorsal nerve was anastomosed to the motor nerve to the vastus medialis. FMT, functional muscle transfer; LD, latissimus dorsi.

associated with the longest median time to maximal neuromuscular recovery (16.8 months), followed by the LD (7.8 months) and gracilis (4.9 months).

The effect of adjuvant therapy on outcomes of FMT is controversial. Previous studies demonstrated that radiotherapy causes intimal vessel damage that negatively affects microvascular outcomes.[47] Muramatsu et al[45] showed that chemotherapy administration leads to a significantly delayed period of reinnervation in a rodent FMT model. In the present study, postoperative chemotherapy was associated with considerably lower muscle power. Additionally, receipt of preoperative chemotherapy or radiotherapy was associated with an increased risk of complications. Patients receiving chemotherapy and/or radiotherapy may have significantly larger and higher grade tumors, necessitating more extensive resections, which may contribute to a higher complication rate.[48] Additionally, many of the commonly used chemotherapeutic agents for sarcoma are neurotoxic and can contribute to poor wound healing.[49–51] While oncologically effective, agents such as anthracyclines and ifosfamide may impair neuron growth, delaying

Table 6 Surgical outcomes in the institutional case series

Characteristic	No. of patients (%)
Median MRC score (IQR)	5 (3–5)
Median time to first neuromuscular function, mo, median (IQR)	1.5 (1.1–2.3)
Median time to maximal neuromuscular function, mo, median (IQR)	7.6 (5.3–12.2)
Complications	7 (54)
Reoperation	1 (8)
Donor-site complications	
Seroma	1 (8)
Delayed wound healing	1 (8)
Recipient-site complications	
Arterial thrombosis	1 (8)
Infection	3 (23)
Seroma	1 (8)
Wound dehiscence	1 (8)

Abbreviations: IQR, interquartile range; MRC, Medical Research Council.

reinnervation of the FMT, resulting in worse outcomes and higher complication rates compared with patients not requiring chemotherapy.

This study has several limitations, most notably the small number of patients undergoing FMT for tumor defects. This calls attention to the fact that these oncologic defects are incredibly rare, even at a large international cancer center such as M.D. Anderson. It is for this reason that we decided to include a formal systematic review and meta-analysis with our chart review, to include as many patients as possible in our analysis. Limitations identified in our systematic review and meta-analysis include the relative heterogeneity of the included studies and the high OCEBM scores; for this reason, we used a random-effects model to minimize the confounding effects of data heterogeneity as much as possible. Limitations in our chart review include the retrospective nature of the study, recall bias, and selection bias. Lastly, we did not include patient-reported outcome measures, which are important considerations in outcome evaluation.

Conclusion

Oncological reconstruction following soft-tissue tumor resection remains a challenge. As demonstrated by our analysis, FMT after oncological resection may improve extremity function after limb-sparing tumor resection. Larger donor muscles such as the LD and VL are more appropriate for lower extremity reconstructions and proximal upper extremity (elbow/shoulder) defects, whereas the gracilis may be more appropriate for wrist and/or finger FMTs. Careful consideration of risk factors and preoperative planning is imperative for successful outcomes.

Conflict of Interest
None declared.

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