RESEARCH ARTICLE

Is Masquelet Technique A Successful Viable Treatment In Reconstructing Large Tumor Bone Gaps in Adolescent and Adult?

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Abstract

Objectives: The reconstruction of large bony defect caused by tumor resection can be managed by different technique like bone graft, Masquelet technique, mega-prosthesis etc. Literature lacks studies discussing Masquelet technique in tumor cases especially pertaining to infected tumor in adults. We aimed to determine 1) How often and how fast is the bone healing achieved after resection greater than 10 cm bone in tumour patient's using Masquelet technique?, 2) Whether Masquelet technique can achieve optimum outcomes in adult infected cases too?

Methods: We reviewed 154 patients of benign & malignant tumour managed by us between 2013 and 2019. Patients belonging to all the age group with infected tumor/diaphysial tumor/periarticular tumor, where single stage surgery or mega-prosthesis is not a viable option and were treated with Masquelet technique for reconstructing a bone defect of at least 10 cm were included in our study. We evaluated outcomes of eight patients for four parameters i.e. bony union, healing index, number of re-do surgeries required and limb length discrepancy.

Results: Mean age of our study group was 20.25 years and patients followed for mean duration of 3.36 years. Mean bone loss after tumor resection was 13.1 cm (range = 11.5 cm to 15 cm). There was no sign of recurrence of tumor in any patient at the time of last follow up. Average time required to achieve bony union was 23.25 months (mean healing index of 1.67 months/cm). All but one patient achieved bony union. Mean limb length discrepancy seen was 1.44cm. Infected cases showed low healing index with higher percentage of re-do surgeries.

Conclusion: Induced membrane technique is quick, safe and reliable alternative method of reconstruction to mega-prosthesis in cases with all age group where risk of failure of mega-prosthesis is high, either due to infection or shorter expected lifespan of prosthesis. However, obtaining union can be a difficult preposition in infected tumor cases and multiple surgeries may be required to get the desired result even after two stages. However, a comparative study with large sample size is required to further validate our results.

Level of evidence: IV

Keywords: Adult age, Chemotherapy, Diaphysial tumour, Induced membrane technique, Infected tumor, Masquelet technique, Mega-prosthesis

Introduction

Aggressive appendicular skeleton tumors deserve special surgical planning on the part of surgeon where most common management is limb salvage by wide resection and surgical reconstruction.[1] Various reconstructive options for such large bone defects include autologous iliac/fibula grafts, autologous vascularized fibula transplantation, induced membrane technique of Masquelet, ilizarov's bone transport, extra-corporeal irradiated autograft, chondrodiastasis, massive allograft and tumor joint replacement.[1-3] Despite each procedure

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having pros and cons of its own, autograft is still considered gold standard as allogenic bone graft have more complications and ilizarov's bone transport method has low compliance due to cumbersome construct.

Metallic mega-prosthesis can tackle this problem where instead of regenerating bone it replaces the bone.[4] Complications associated with mega prosthesis can be mechanical or non-mechanical. Mechanical problems like aseptic loosening, prosthesis fracture and soft tissue attachment failure are steadily decreasing due to improvement in designing and modularity.[5,6] Non-mechanical complications are more serious; which include infection, poor wound healing and relapse of tumor. Hence, biological reconstruction is usually favored in patients with long term survival.[7]

The two stage induced membrane technique described by Masquelet was incidentally discovered in 1986. It has been studied extensively in post-traumatic diaphyseal bone defects.[8] in first stage; the bone defect is filled with cement spacer, which is followed by second stage after 4-6 weeks in which cement spacer is replaced by bone graft. In 4-6 weeks, a psuedosynovial membrane develops around the cement spacer due to foreign body reaction. This membrane acts as a biological chamber, which secretes growth factors, which are osteogenic, and angiogenic that not only helps in prevention of graft resorption but also promotes its corticalization and vascularization after second stage. Apparently, it is a rather simple and time effective procedure, but its role in bone tumor is less explored yet.[9]

Moreover, there is paucity of literature of this technique being used in managing post-tumor resection bone gap in adult patients and in infected tumor scenarios even including tumors like giant cell tumor. We hypothesize that Masquelet technique should also reproduce optimum results in adult tumor patients especially with infected tumors. Hence, in this study we report our experience of Masquelet technique in management of these two unique scenarios and we aim to know how often and how fast is the bone healing achieved after resection greater than 10 cm bone in tumor patient's using Masquelet technique and whether Masquelet technique can achieve optimum outcomes in adult patients too specifically in infected tumor cases?

Materials and Methods

Data of all patients diagnosed with bone tumor between 2013 and 2019 were reviewed. We treated 154 patients including benign and malignant tumor using various treatment options depending on type and staging of the tumor. All the tumor patients irrespective of their age, if found unsuitable for treatment of tumor by either mega-prosthesis or single stage definitive management were managed by induced membrane technique and followed for minimum 18 months were reviewed for this study. Of these 154 patients, only eight patients were managed by induce membrane technique and had massive bone loss (>10 cm) secondary to tumor excision.

The inclusion criteria for which patients primarily managed with Masquelet technique were:

1) Infected tumor with frank signs of infection or tumor with fungating mass
2) Diaphyseal tumors
3) Periarticular tumors where mega-prosthesis is not a good option either due to non-availability of standard implant (wrist joint) or not very successful (elbow and ankle joints and in very young children).

All other patients i.e. 146 patients were excluded from the study who were either managed conservatively, or managed by any other treatment option like curettage and bone grafting, single stage excision and bone grafting, arthrodesis or mega-prosthesis and even amputation.

This research has been approved by IRB of our institution and approval was taken prior to conducting retrospective analysis of patient's outcomes and prior consent from all the patients were also taken for use of their records for research and publication. As our study is a retrospective study and because we have concealed the identity of the patients, formal ethical committee clearance was not required in our institution.

Reconstruction of bone defect was performed in two stages as described by Masquelet. Tumor resection was performed by single surgeon (LM) as per the principles of limb salvage in musculoskeletal malignant tumors after preoperative workup to plan the surgery and to rule out metastasis.[10]

In stage one, antibiotic PMMA cement spacer was inserted in the defect created after tumor resection and stabilized by internal and/or external fixation. Whenever possible, fixation with a long intramedullary device was preferred for optimal stability. Locking plate or TENS (Titanium Elastic Nailing System) nails were used when locking nail was considered unsuitable. External fixator was added for additional stability in cases where optimal stability was not obtained with internal fixation devices. Wherever possible especially at diaphysis, precautions were taken to create a good contact between cement and bone by wrapping the cement around the bone, which can allow surgeon to lift small piece of bone with membrane during second stage. Second stage was performed after a time gap of eight weeks after first surgery.

In patients who received adjuvant chemotherapy, the second stage was done after a gap of six to eight weeks after completion of chemotherapy. Membrane was opened using longitudinal incision. After careful extraction of bone cement the gap is filled with bone, either cortical &/or cancellous bone graft obtained via autograft, allograft or both depending upon the requirement and availability. Due care was taken to suture the membrane back close to the bone graft after putting the graft inside the membrane.

Outcomes of eight patients were evaluated and reviewed in this study [Table 1]. Out of Eight patients, five patients received pre and post-operative chemotherapy and three patients with giant cell tumor did not receive any chemotherapy.

Outcomes were divided into two broad categories i.e. Primary and secondary; in which complications like infection, non union were observed and evaluated as a secondary outcomes [Table 2].

Table 1 – Patient demographic data with surgical details

Group	Case	Age	Sex	Site	Diagnosis	Bone loss (in cm)	Implant for stage 1	Gap between two stages	Second stage
A (Infected)	1	15	M	Proximal tibia Metaphysis	Fungating Telengectatic Osteosarcoma	15	K-Nail With Knee Spanning Ex-Fixator	5 months	Cement Spacer Removal + Fibular Grafting
	2	22	M	Proximal tibia Epipysio-Metaphysis	Recurrent GCT with Discharging Sinus	13	K-Nail	2 months	Implant Removal + Bone Grafting + Long Nail (Knee Arthrodesis)
	3	25	M	Distal Tibia Epiphysis	Fungating Recurrent Malignant GCT	12	Schanz Screw With Ankle Spanning Ex- Fixator	2 months	Spacer Removal +Bone Grafting+ Fibulectomy And Ankle Arthrodesis
B (Non-infected)	4	15	F	Distal Humerus Epiphysis	Malignant GCT	12	Schanz Screw	2 months	Spacer Removal+ Bone Grafting+Humero-Ulnar Plating(Elbow Arthrodesis)
	5	12	M	Femur Diaphysis	Ewings Sarcoma	11.5	K-Nail	4 months	Spacer Removal +Bone Grafting
	6	17	M	Proximal tibia Metaphysio-Diaphysis	Ewings Sarcoma	14.5	Proximal Tibia Plate	5 months	Spacer Removal+ Bone Grafting
	7	7	F	Ulna Diaphysis	Ewings Sarcoma	14.5	Tens Nail	5 months	Spacer Removal + Bone Grafting
	8	45	F	Radius Epiphysio-Diaphysis	Ewings Sarcoma	12.5	Tens Nail	4 months	Spacer Removal + Bone Grafting+ Wrist Arthrodesis

Table 2 – Observation and results of Assessment Parameters

		Diagnosis	Follow - up period	Complication of stage 1 surgery	Complication 2nd surgery	Duration to heal	Healing index (months/ Cm of gap)	Cases Required Redo surgeries to achieve union	2nd stage bone graft site	Allograft used	Successful bony Union (after both primary and redo surgeries)	Limb length discrepancy (cm)
A Infected	1	Fungating Telengectatic Osteosarcoma	HBsAg Positive	Infection And Non Union	6.5 years	66 months	4.4	1. Implant removal, debridement and cement beads 2. Beads removal & Ilizarov ex fixator 3. Corticotomy	Fibula C/L	no	No (final outcome -stiff non-union)	2.5
	2	Recurrent GCT Discharging Sinus	Nil	Non Union	3 years	18 months	1.38	1. Implant removal + knee spanning ring fixator	Patella And C/L Fibula	no	yes	2
	3	Fungating Recurrent Malignant GCT	Nil	Poor Wound Coverage	1.5 years	9 months	0.75	1. Skin grafting after 3 weeks of VAC therapy for wound coverage	C/L Iliac Crest	no	yes	1
B Non-infected	4	Malignant GCT	Nil	Nil	5 years	9 months	0.75	no	Fibula	no	yes	1
	5	Ewings Sarcoma	Nil	Nil	4 years	18 months	1.57	no	Bilateral Fibula	yes	yes	3.5
	6	Ewings Sarcoma	Nil	Non Union And Implant Failure	4 years	42 months	2.9	1. Implant removal + Bone grafting with Allograft & re-osteosynthesis)	C/L Fibula And Iliac Crest	yes	yes	1
	7	Ewings Sarcoma	Nil	Nil	1.5 years	12 months	0.62	no	Allograft	no	yes	0.5
	8	Ewings Sarcoma	Ventral Dislocation Of Spacer	Nil	1.5 years	12 months	0.96	no	Iliac Crest And Fibula	no	yes	0

Parameters assessed Primary outcomes were

1) Bony union was considered as primary outcome measure for assessment. The procedure was deemed successful if the bone healed without any further surgical intervention after second stage. Oncological follow up was done every month for first six months and then three monthly till bony union followed by six monthly radiographs. Each patient was assessed for bony union using AP and lateral radiographs of the involved area. Minimum of three cortex union out of four cortexes in two radiographs was considered as bony union.[11]
2) Healing index for each patient was calculated, which is length of bone gap healed in centimeters divided by number of months taken to achieve complete bony union.[12]
3) In cases where bony union did not occur or was considered delayed, add on surgical procedures were done to achieve bony union. Hence, the number of surgeries required to achieve bony union after second stage was labeled as a secondary outcome measure.
4) Limb length discrepancy

Eight patients were included in our study for analysis of results. Primary and secondary outcomes were evaluated by descriptive statistical analysis using SPSS 22.0 software.

Results

Age group of our study population was from 11 years to 45 years of age (mean age = 20.25 years). Five out of eight patients were male while remaining three were females. Two patients out of three patients of GCT i.e. case no "2" & case no. "3" were treated somewhere else initially and presented to our hospital as a case of recurrent GCT [Table 1]. All patients had successful surgical excision of tumor as histological examination of the excised bone specimen of all patients had negative surgical margins for tumor cells after first stage. Mean bone loss after tumor resection was 13.1 cm (range = 11.5 cm to 15 cm). Time gap between two stages ranged from two months to five months depending upon adjuvant chemotherapy duration. Patients were followed up from 1.5 year to 6.5 years (Average follow up= 3.36 years). There was no sign of recurrence of tumor in any patient and all patients were free of disease at the time of last follow up [Table 1].

Average time required to achieve bony union was 23.25 months. While minimum time required was nine months in case no. "3" and "4"; and the maximum time taken was 66 months by patient of telengiectatic osteosarcoma i.e. case no. 1 who achieved optimum function of limb with stiff non-union. The average time to bony union in infected group was 31 months while it was 18.6 months in non-infected group. Overall, mean healing index was 1.67 months/cm (range 0.62 months/cm - 4.4 months/cm with standard deviation 1.32). Average mean healing index in infected group was 2.18 months/cm while in non-infected group it was 1.36 months/cm. Five out of eight patients had bony union after second stage of Masquelet technique i.e. without any other surgical intervention (re-do surgery) to achieve union. All cases except Case no."1" had union if surgical interventions after second stage were taken into account. Case no. "1" with diagnosis of telengiectatic osteosarcoma developed stiff non-union.

Average numbers of re-do surgeries required for bony union in infected group (including patient "1" with stiff non union) was 1.67 compared to non-infected group where the average number of redo surgeries were 0.2. Patient Case no. "1" still has stiff non-union despite three redo surgeries [Figure 1A – 1D]. Despite stiff non union, patient walks comfortably without using brace/assistive device with no functional deficit [Video supplement 1]. Good function and psychological satisfaction was achieved in case no. "1" i.e. telengiectatic osteosarcoma, after developing stiff non-union which restrained surgeon to opt for further multiple surgeries to achieve bony union [Figure 2A, 2B]. We were able to achieve arthrodesis in all patients where it was intended so. One out of three patient of giant cell tumor (Case no. "2") required additional surgery to achieve bony union, while other two patients showed bony union after second stages of Masquelet technique in nine months duration [Figure 3A – 3D]. Limb length discrepancy was seen in all the patients with mean LLD of 1.44cm (ranging from 0 cm to 3.5 cm), however average limb length discrepancy was two cm in lower limb patients, which is considered within well tolerated limits [Table 2].

Problems like number of re-do surgeries, LLD; were more in infected group as compared to non-infected group. Secondary Outcomes including various complications encountered in our study like infection, non union, poor wound coverage was seen after stage two in one patient of GCT i.e. Case no. "3" which was managed accordingly [Figure 4A, 4B; Table 2].

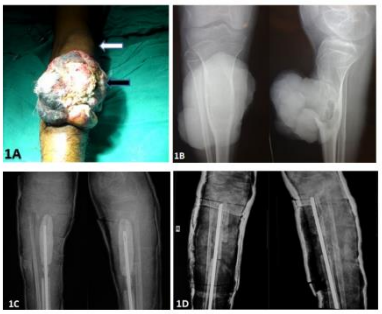

Figure 1. Case no. 1 - Telengiectatic osteosarcoma/ Figure 1A – Pre op Clinical picture of Case no. 1 Telengiectatic Osteosarcoma, white arrow pointing knee joint and black arrow pointing fungating tumour/ Figure 1B – Pre op X-ray AP and Lateral view of Case no. 1 Telengiectatic Osteosarcoma/ Figure 1C – Post op X-ray AP and Lateral view after stage 1/ Figure 1D – Post op X-ray AP and Lateral view after stage 2

Figures 2A – Final follow up X-ray AP and lateral view demonstrating non union of Case no. 1 Telengiectatic Osteosarcoma/ Figure 2B – Clinical photograph showing aesthetic limb with good function of Case no. 1 Telengiectatic Osteosarcoma (from left to right showing knee flexion, active SLR and limb length discrepancy)

Figure 3 – Case no. 3 – Fungating Recurrent Giant cell tumour/ Figure 3A – Pre op Clinical picture of Case no. 3 Fungating Recurrent GCT/ Figure 3B – Pre-op X-ray AP and Lateral view of Case no. 3 Fungating Recurrent GCT/ Figure 3C – Post-op X-ray Lateral view after stage 1/ Figure 3D – Post op X-ray AP and Lateral view after stage 2

Figure 4A – Follow up X-ray AP and Lateral view demonstrating bony union of Case no. 3 Fungating Recurrent GCT (arrow pointing the bridging callus in both the views)/ Figure 4B – Clinical photograph of finally healed limb after skin grafting of Case no. 3 Fungating Recurrent GCT

DISCUSSION

Induced membrane technique was described by Masquelet et al to address the issue of critical size bone defect in adults. Masquelet technique was actually described for traumatic segmental bone defects using cancellous graft.[13] Our current study highlights the use of this technique in managing post tumor resection bone defects in adults and adolescent especially in cases where single stage surgery or mega-prosthesis is not available, not successful or not indicated like in cases with active infection either locally or systemic, poor soft tissue condition locally, fungating tumor mass which are labeled as infected tumors.[7] Though, few authors have used this technique in young patients or children that too mainly in diaphysial tumors without any infection. It is imperative to highlight that our study is first of its kind which discusses the outcomes of Masquelet technique in adult patients with infected tumors or unsuitable reconstruction with mega-prosthesis till date in literature. Furthermore, our series extended the spectrum of use of Masquelet technique by discussing the outcomes of this technique in patients with GCT.

As in other series, to minimize the risk of infection and poor wound healing associated with chemotherapeutic drugs; we modified this technique in our patients who received adjuvant chemotherapy by delaying the second stage.[14-16] Adjunct cortical graft was not advisable by Masquelet et al. who suggested that two third of the graft should be autologous cancellous bone graft.[13] We had to use fibula cortical strut grafts and allograft to tide over the issue of limited cancellous autograft available in comparison to the size of bone defect. Despite the changes (i.e. duration between first and second stage) made to this technique the induced membrane did help in integration of bone graft efficiently as highlighted by good union rate despite a huge bone defects. Moreover, we experienced that even after 4-5 months gap between 1st and 2nd stage of Masquelet technique, biological membrane was seen over the cement spacer in our study in five patients i.e. case number "1, 5, 6, 7 and case no. 8" [Table 1]. Presence of biological membrane even after 4-5 months suggest that delayed second stage can also be successful if done correctly, which embarks an important development in evolution of induced membrane technique. However, our subjective observation requires a histological testing of such biological membrane formed after five months of interval to comment and validate whether the biological membrane functions similar to what has been described by Masquelet.

Various authors has done studies evaluating results of induced membrane technique in tumour patients pertaining to children or adolescent and showed promising results. As literature lacks any such study on adult, we compared result of our study with all such studies to evaluate the efficacy of Masquelet technique in adult population if compared with paediatric age group.

In our study, five out of eight patients achieve union when no redo surgeries were considered which is similar to that shown by Jean-Charles Aurégan et al (58%) in their systemic review, suggesting satisfactory outcome in adolescent and adult age group patient, though time to union is more and case "1" took even longer time for achieving satisfactory results.[17] After considering redo surgeries for outcome, seven patients out of eight achieved union which is similar to Jean-Charles Aurégan et al. where the union achieved was in 87% when redo surgeries were taken into consideration. Average time to bone union after second stage in our study was 19.6 months (including patient "1" who had stiff non union and is functionally doing good without any support) while it was 9.5 months in a study by Guoron et al in a series of children with varied etiology.[18] Healing index was 1.67 months/cm of regenerate in our study compared to 0.31 months/cm in a study by Fitoussi et al., [12] who conducted his study of tumor excision limited to children and adolescent. Different healing index can be understood on the basis of difference in healing potential between children and adult and as our study included adult patients too, hence healing index is more than what can normally be seen in young age group patients.

Non union was seen in three out of eight cases. Two of these had non union at distal end and one had nonunion at both ends. However, union was achieved in all except patient case "1" even after iterative surgeries in our study.

Our result of union corroborates with the similar studies in literature to a greater extent. Ten out of eleven cases in a study by Villemagne et al. did not achieve union after second stages of Masquelet technique but union was achieved in all after at least one further surgical procedure.[15] Guoron et al. reported a non union rate of 35% in their case series of 13 children.[18] Junctional pseudo-arthrosis has been shown to occur in 30% to 100% cases depending upon the case series.[15, 16, 18]

Two most important causes of non union mentioned in the literature are unstable fixation and technical errors where the bone ends are not covered with cement sleeve during stage one surgery.[18, 19] In our study insufficient coverage of cement sleeve may be the case of non union in two cases but infection appears to be a cause of non union in one patient [Table 3].

TABLE 3. COMPARATIVE ANALYSIS OF PREVIOUS CASES SERIES

Study	Number of patients	Children/adult	Broad category of diagnosis in which Masquelet performed	Non Union	Infections	Average time to bone union
Fitoussi F et al. 2015 {12}	08	Children [mean age 13 years (11-17)]	Tumour	3 cases	2 cases	5.6 months
Villemagne T 2011 [15]	11	Children [mean age 9 years (3-15.5)]	Tumour	7 cases	none	11.5 months
Gouron R et al. 2013 [18]	14	Children [mean age 10.6 years (11-17)]	Mixed (tumour, trauma, congenital)	5 cases	2 cases	9.5 months
Chotel et al 2012 [16]	08	Children [mean age 12.1 (7.5-18 years range)]	Tumour	2 cases	1 case	4.8 month (excluding 1 case)
Accadbled F. et al. 2013 [26]	03	Children [mean age 6 year (3-9 years)]	Tumour	All cases	-	-
Mansour et al. 2017 [27]	09	Children	Mixed (tumour, congenital)	2 cases	2 cases	8 months (excluding 2 cases – 1 died, 1 union in progress)
Current study Sharma A et al. 2022	08	Adolescent and adult [mean age 20.25 years (11-45)]	Tumour	3 cases	1 case	19.6 months (including 1 outlier case took 66 months)

Infection rate in our series after performing Masquelet technique was seen in one patient out of eight. Prevalence of infection ranges from 7.5% to 13% after segmental allograft.[20-22] Infection rate was even higher i.e. 10%-15% after using vascularized fibula.[22-24] Though infection is in itself one of the complication after Masquelet technique yet a recently published review by Careri et al. suggested this technique as an excellent alternative to solve long bone infected defects by controlling the local infection.[25] In our study too we performed Masquelet technique in three patients with infected tumor and observed good results.

Massive graft resorption is one of the serious complication of induce membrane technique [18,26,27] Accadbled et al. reported massive graft resorption occurring specifically in femur reconstruction.[26] This complication was not seen in our study probably because we enhanced the stability which reduces chances of graft resorption by using non vascularized fibula i.e. cortical graft along with available cancellous graft.

Another common complication seen with this technique is re-fracturing due to poor corticalization of graft.[13, 28-30] Till now we have not encountered this complication in our cases, which may be due to gradual rehabilitation and delayed weight bearing protocol commonly used in our hospital for management of such patients. Though with more long term follow and larger sample size such complication may get acquainted.

Though Masquelet technique was initially described in adult population itself, yet literature lacks studies utilizing this technique in bone tumor among adult age group. One

of the possible reasons of lack of such studies in adult population with tumor may be the apprehension of surgeon regarding increased chances of complication like non-union, re-fracture of regenerate etc. in adults. However, availability of mega-prosthesis can also be one of the reasons. Our study population was heterogeneous with respect to age including adolescent and adults both; suggesting that Masquelet technique can be used successfully in tumor reconstruction surgery in adult patients too with good success rate as shown in our study on long term follow up. However, the complication rate is nearly similar to children, but the duration of treatment can be longer due to slower healing rate of bone defect in adults in comparison to children. Even spectrum of Masquelet technique can be extended to tumors like GCT in which other options of treatment does not appear to be viable.

There are few limitations of study which includes small samples size, heterogenous data and short follow up in three out of eight patients. Even though literature suggests that results are usually stable after bone healing is achieved by biological reconstruction but late complications can be seen with further follow up. Hence, a study with larger homogenous sample size and even longer follow up of all subjects may be required to validate these results.

Conclusion

Induced membrane technique is quick and safe method of reconstruction. However, it must be kept in mind that obtaining union can be a difficult preposition in infected tumor cases and multiple surgeries may be required to get the desired result even after two stages. It is reliable alternative to mega-prosthesis in adolescent and adult age group patients even with varied diagnosis like in recurrent GCT where the ever present risk of failure of mega-prosthesis is high due to longer expected survival of patients. Arthrodesis may prove to be a better option than arthroplasty in such cases.

Keeping in mind our results, we believe that the technique merits further investigation to better define its use compared to other methods of reconstruction.

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