GIANT CELL TUMOUR

DR RAJAT GUPTA

ORTHOPAEDIC ONCOLOGIST

BONE CANCER CLINIC

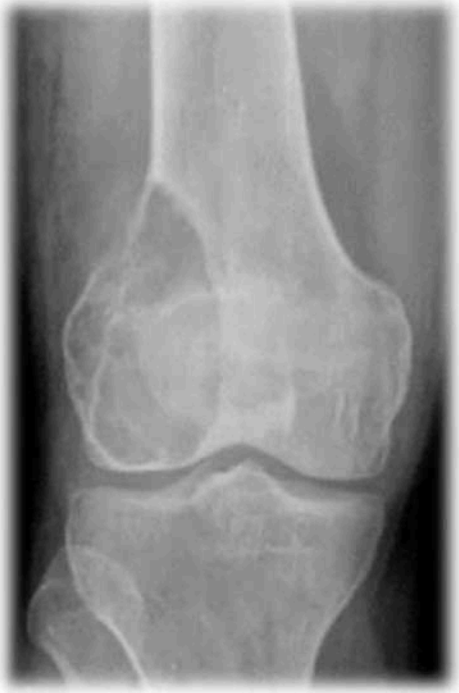
CHANDIGARH

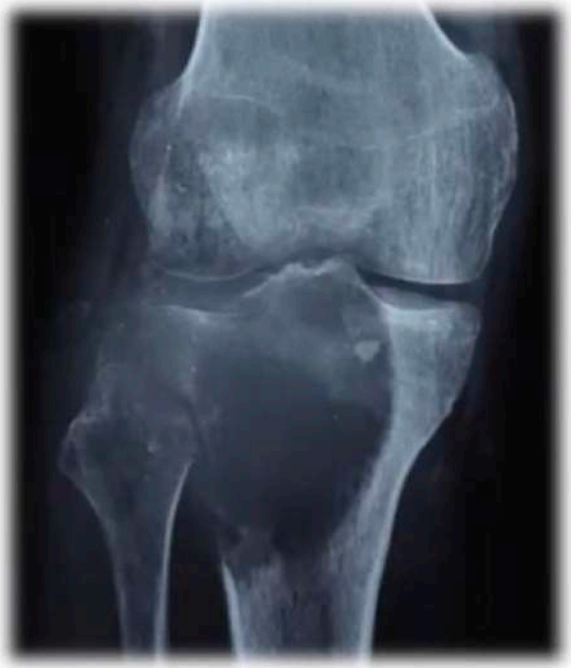
www.curebonecancer.com

+91-9930372264

GIANT CELL TUMOUR

- BENIGN AGGRESSIVE TUMOUR
- 20-40 YEARS
- FEMALE PREPONDERANCE
- 5% OF ALL BONE NEOPLASMS



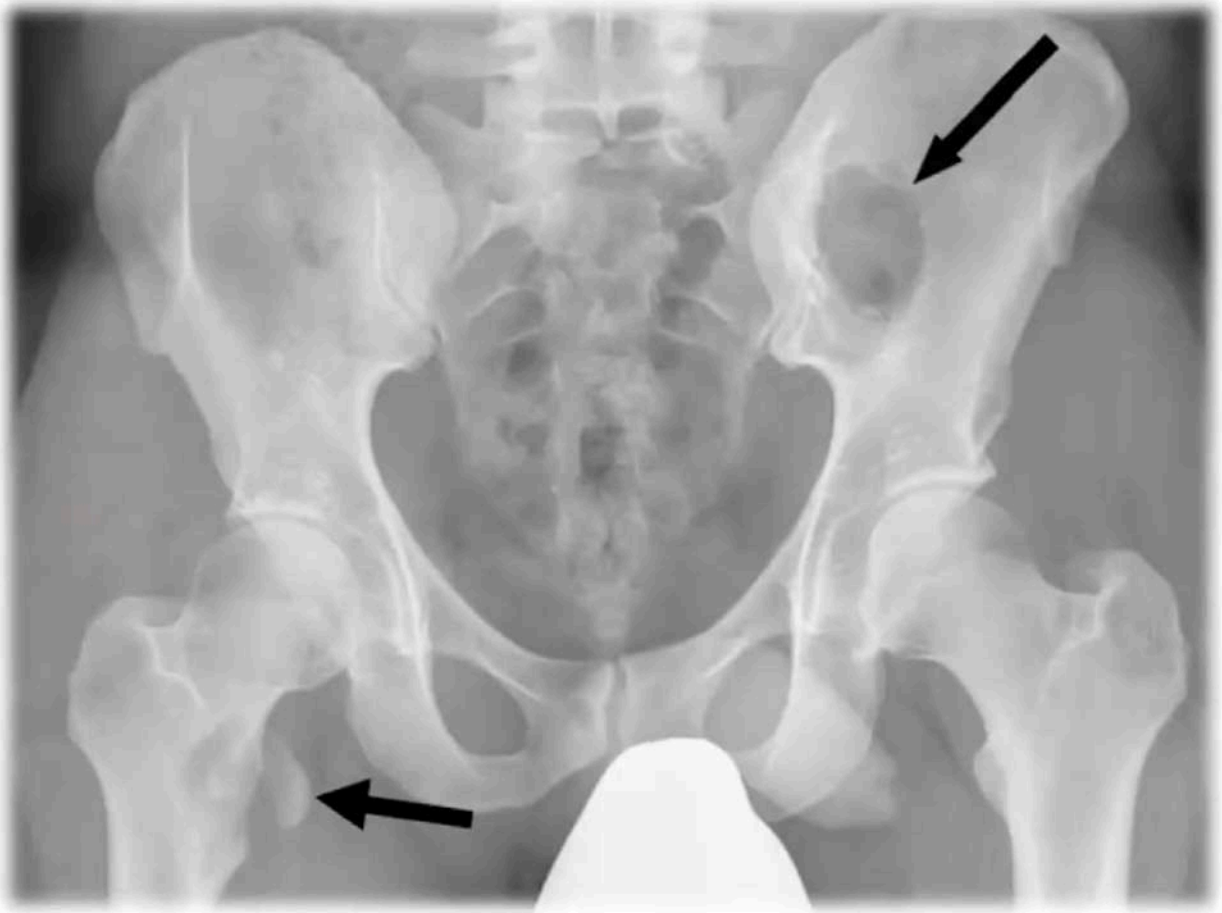


- MORE COMMON IN INDIAN & CHINESE POPULATION

GIANT CELL TUMOUR

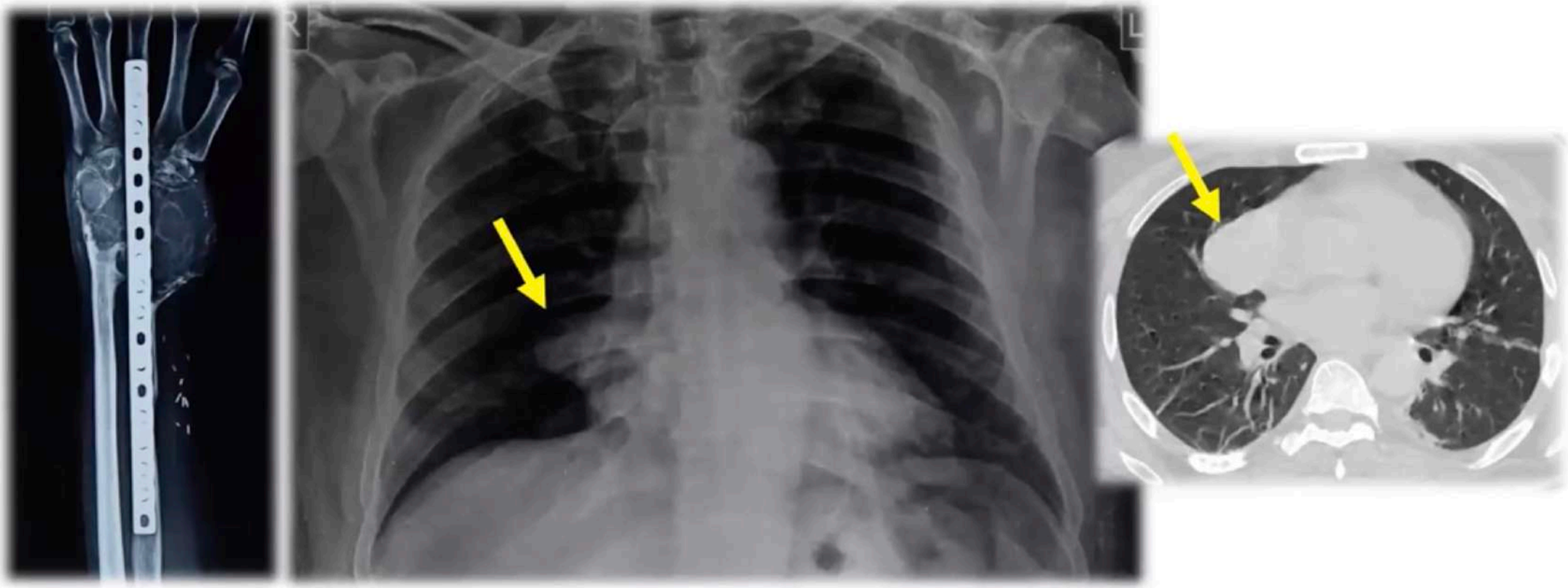
- CAN BE MULTICENTRIC IN 2% OF THE CASES

  - Synchronous
  - Metachronous



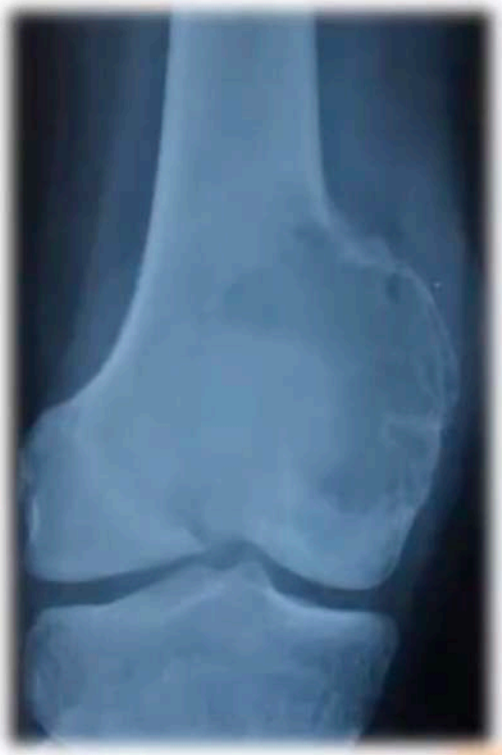
GIANT CELL TUMOUR

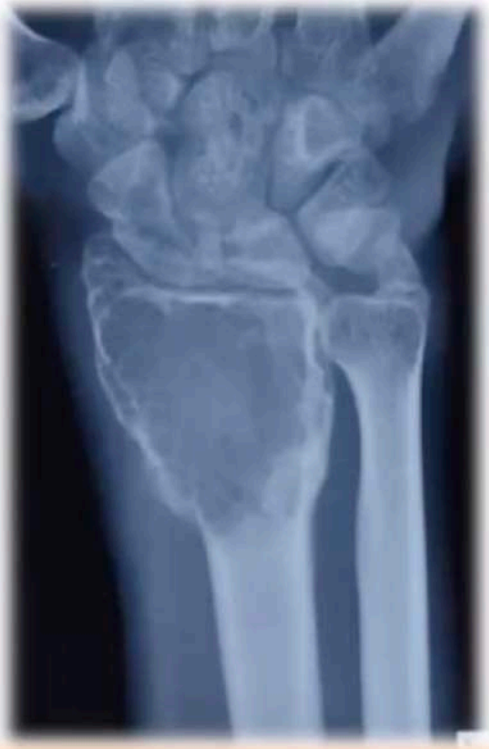
2% OF THE PATIENTS DEVELOP LUNG METASTASIS



MORE SO IN RECURRENT CASES

GIANT CELL TUMOUR

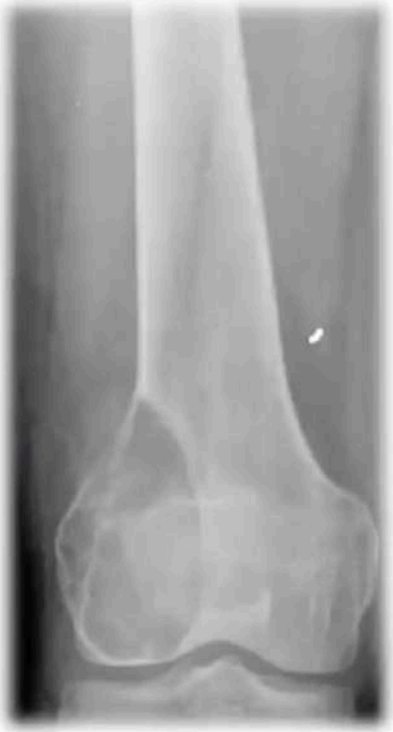


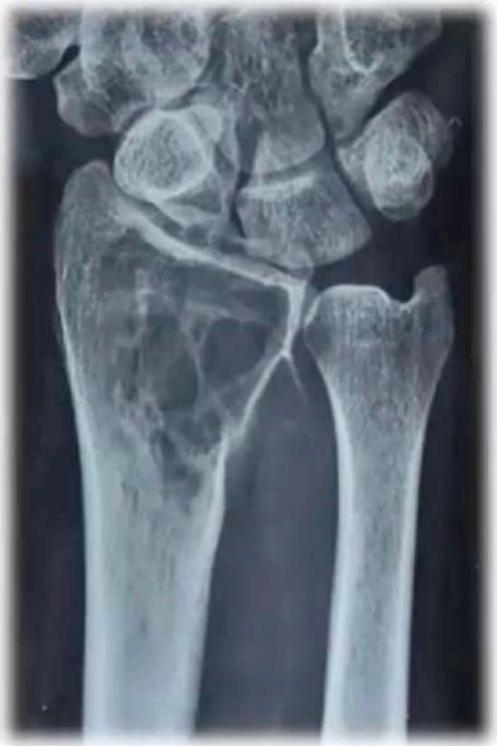


- **AGE** *SKELETALLY MATURE*
- **LOCATION OF TUMOUR** *EPIPHYSEAL*
  METAPHYSEAL IN SKELETALLY IMMATURE
- **TYPE OF LESION** *GEOGRAPHICAL*
  Eccentric
- **MATRIX OF LESION** *NO MATRIX*
- **ZONE OF TRANSITION** *NARROW*
- **TYPE OF PERIOSTEAL REACTION** *NIL*
- **SOFT TISSUE COMPONENT** *CAN HAVE*

ABSENCE OF SCLEROTIC RIM

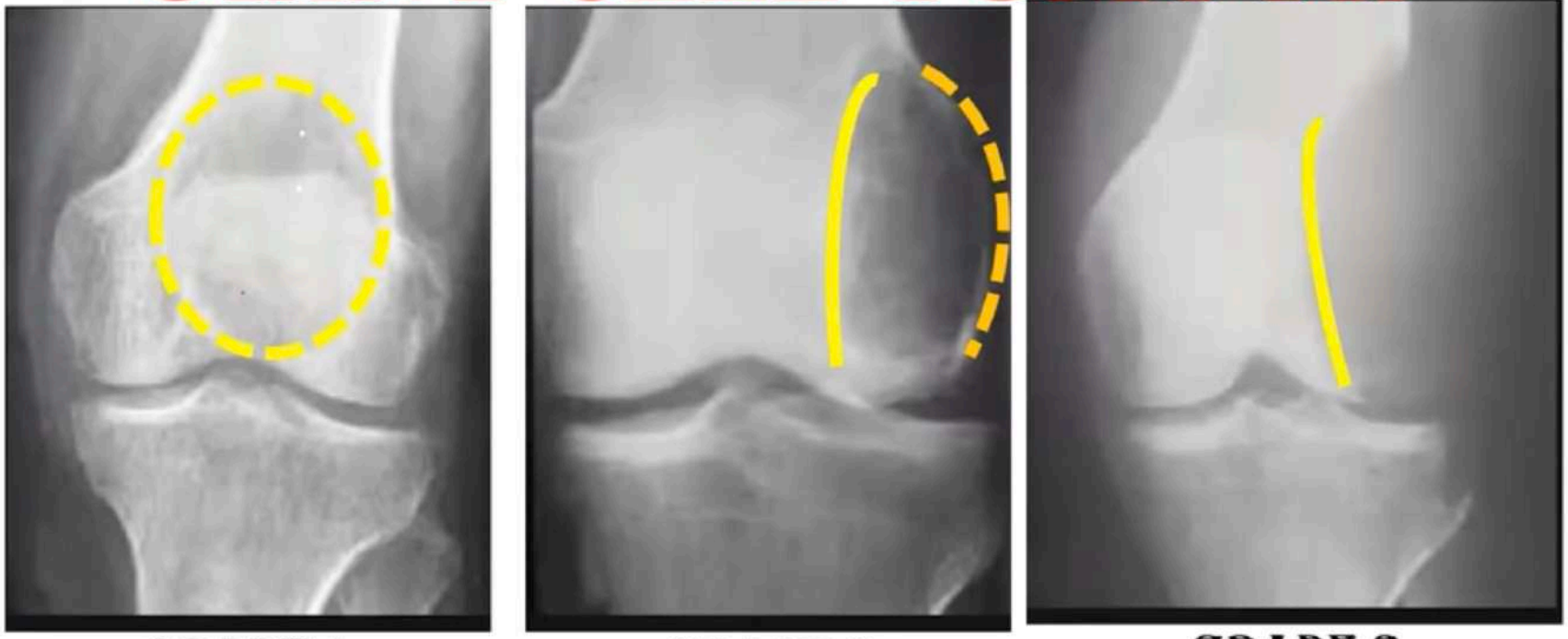
GIANT CELL TUMOUR





SOAP BUBBLE APPEARANCE

GIANT CELL TUMOUR



GRADE 1

Well marginated border

GRADE 2

Relatively well defined margins

Expanded but intact cortex

GRADE 3

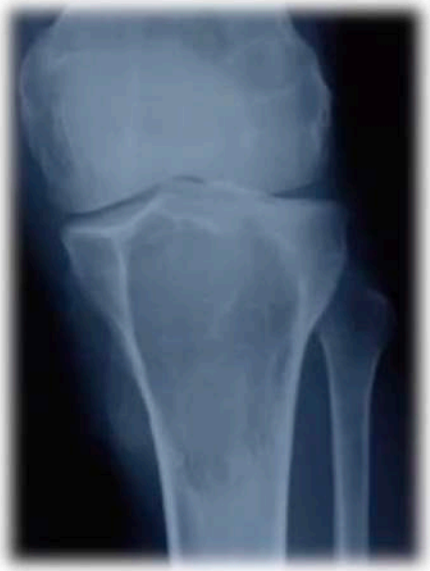
Cortex is broken with soft tissue component

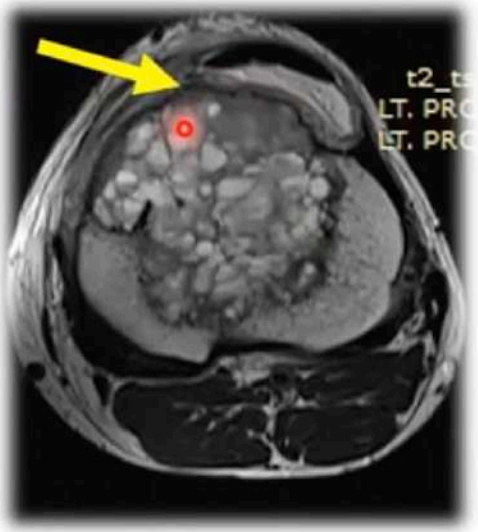
Campanacci grade

GIANT CELL TUMOUR

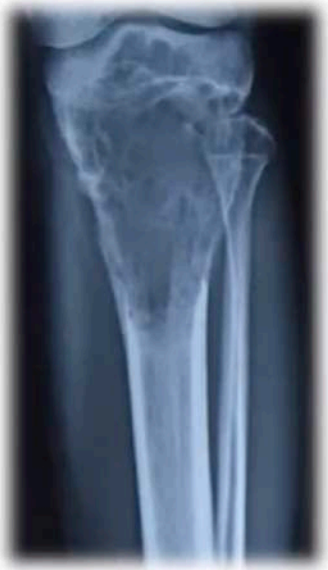
DIFFRENTIALS

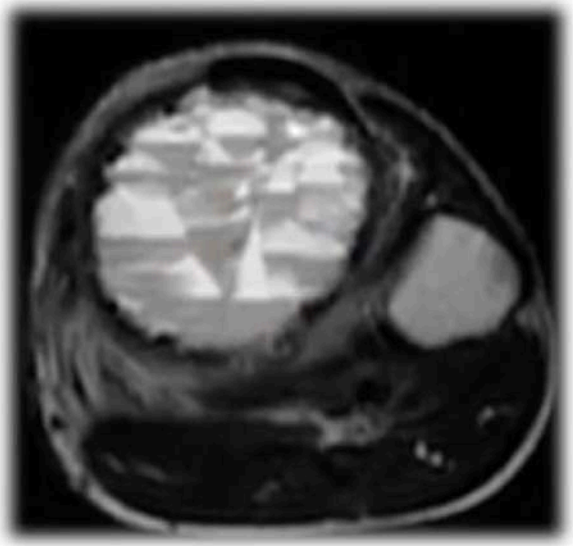
GCT





ABC

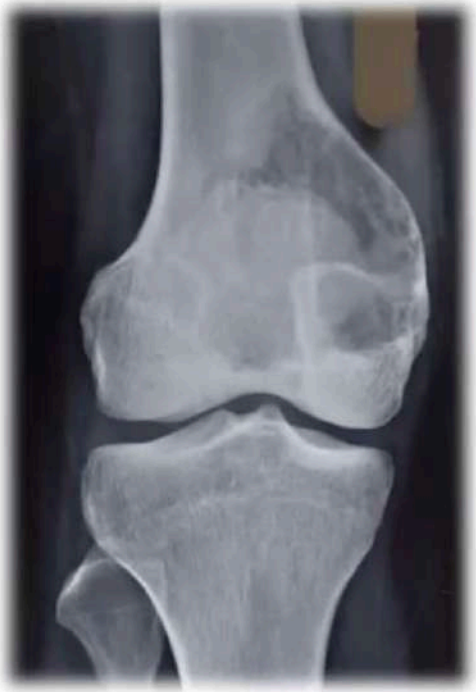




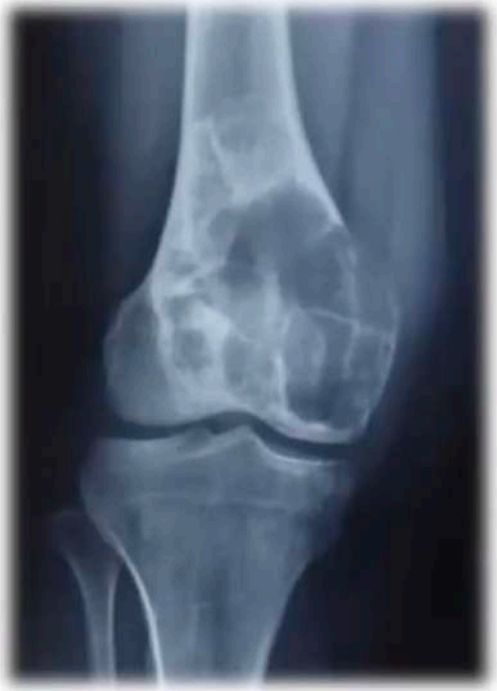
GIANT CELL TUMOUR

DIFFRENTIALS

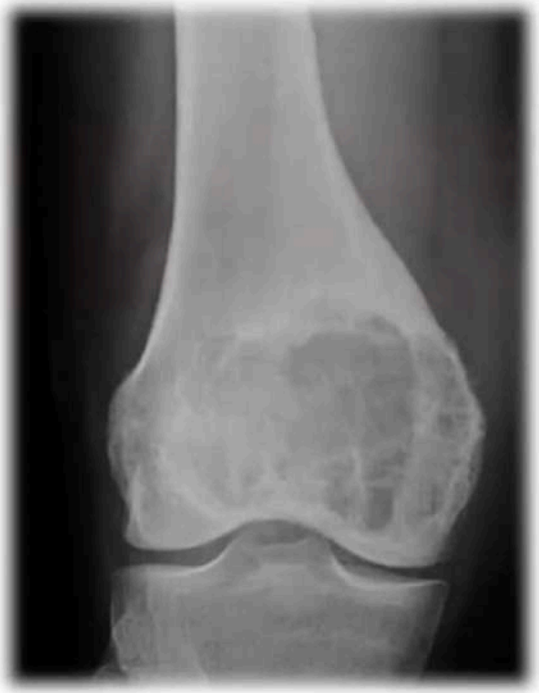
GCT



CLEAR CELL CHONDROSARCOMA



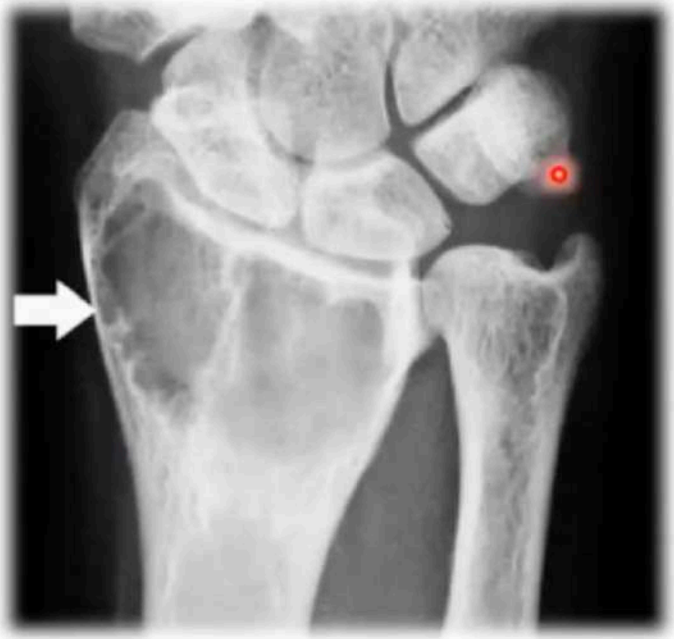
CHONDRO BLASTOMA



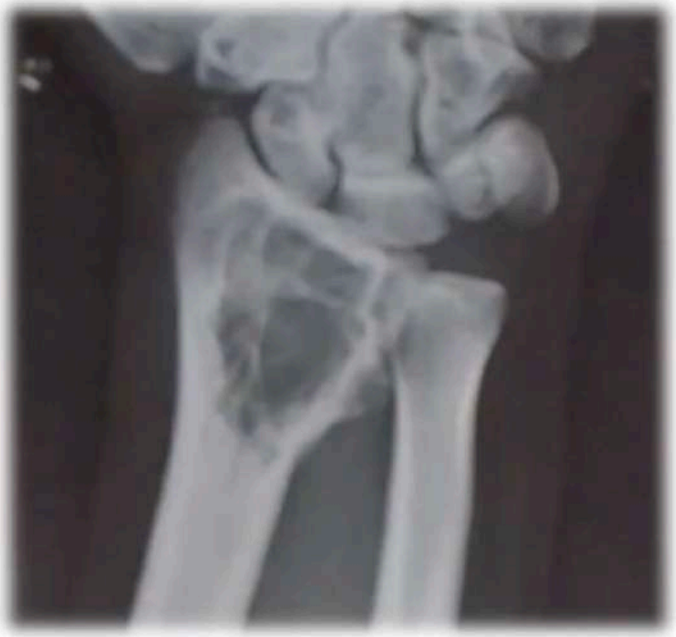
GIANT CELL TUMOUR

DIFFRENTIALS

BROWN'S TUMOUR



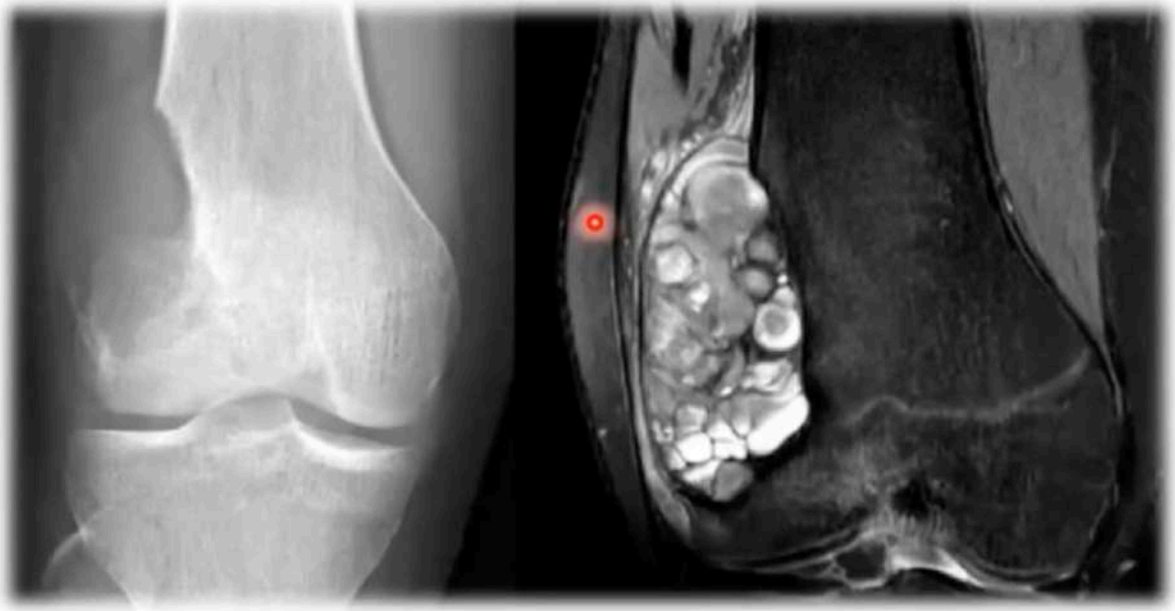
GCT



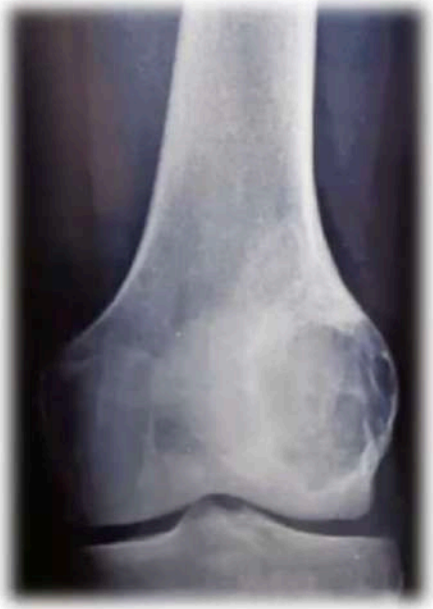
GIANT CELL TUMOUR

DIFFRENTIALS

GIANT CELL RICH OSTEOSARCOMA



GCT

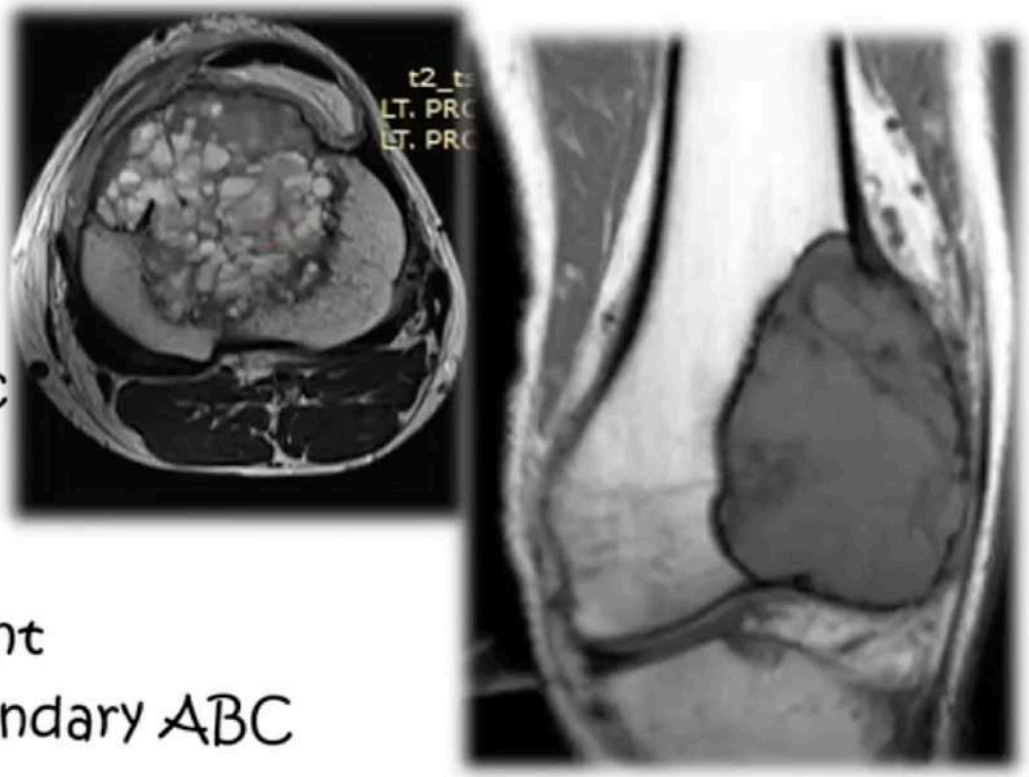


GIANT CELL TUMOUR

WORK UP

MRI

- Epi-metaphyseal region, eccentric
- T1 – Hypointense
- T2 – Hyperintense/ Mixed
- Can have extraosseous component
- Can have Fluid fluid level – Secondary ABC component



GIANT CELL TUMOUR

WORK UP

BLOOD INVESTIGATIONS

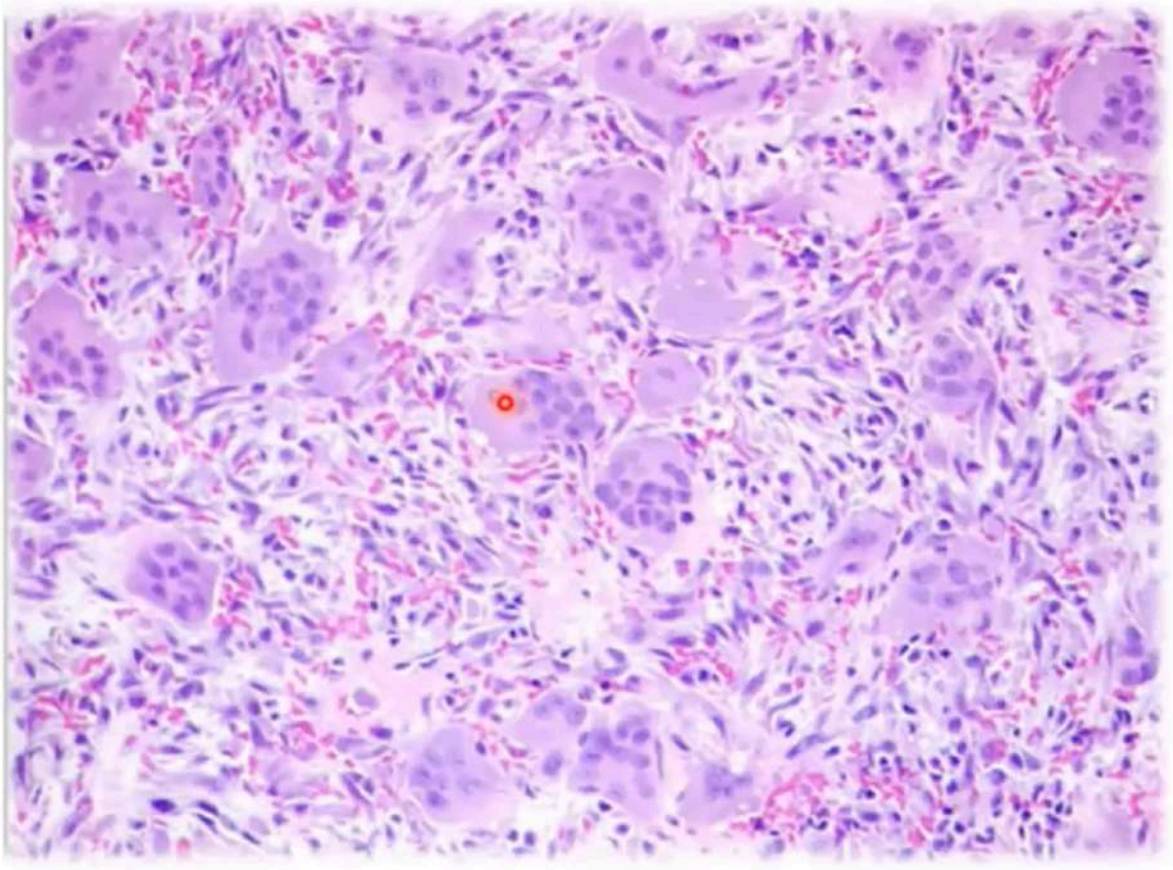
- Serum Calcium levels

GIANT CELL TUMOUR

WORK UP

BIOPSY

GIANT CELL RICH LESION IS NOT SYNONYMOUS WITH GIANT CELL TUMOUR OF BONE



GIANT CELL TUMOUR

TREATMENT

SURGICAL MODALITIES

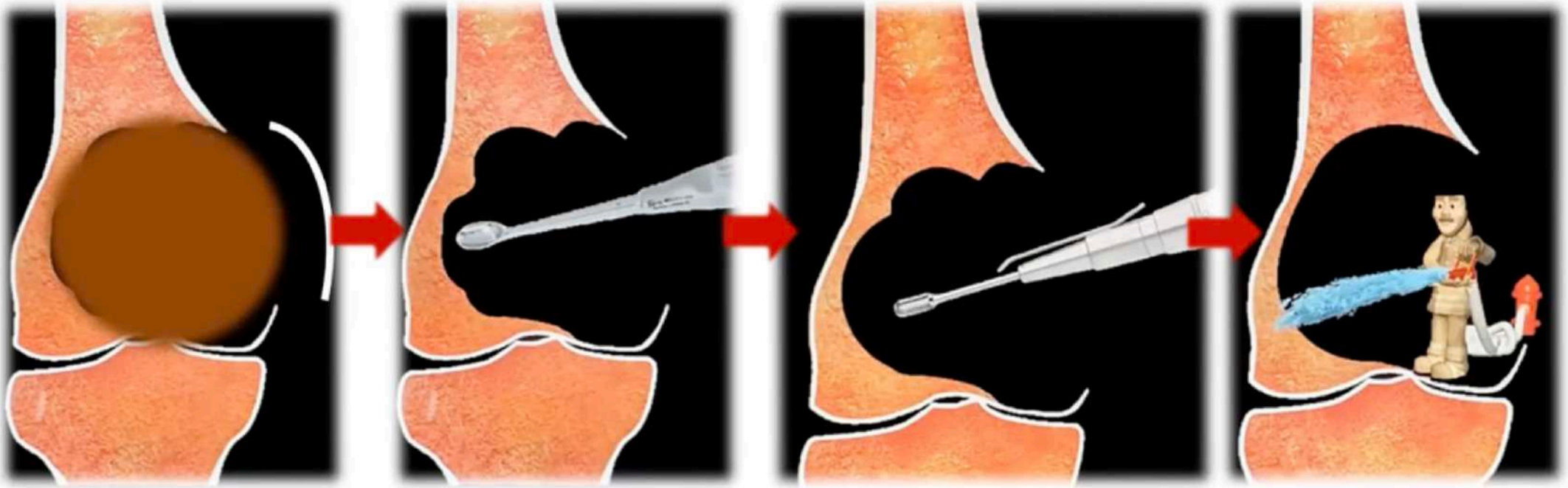
- **EXTENDED CURETTAGE**
- **RESECTION**

NON SURGICAL MODALITIES

- **ANGIOEMBOLISATION**
- **ZOLENDRONIC ACID**
- **DENOSUMAB**

GIANT CELL TUMOUR

CURETTAGE



LARGE WINDOW

SCOOP OUT TUMOUR

HIGH SPEED BURR

PULSE LAVAGE

GIANT CELL TUMOUR

EXTENDED CURETTAGE

≈ LIQUID NITROGEN
- Maximum penetration 14mm
- Fractures
- Nerve injury

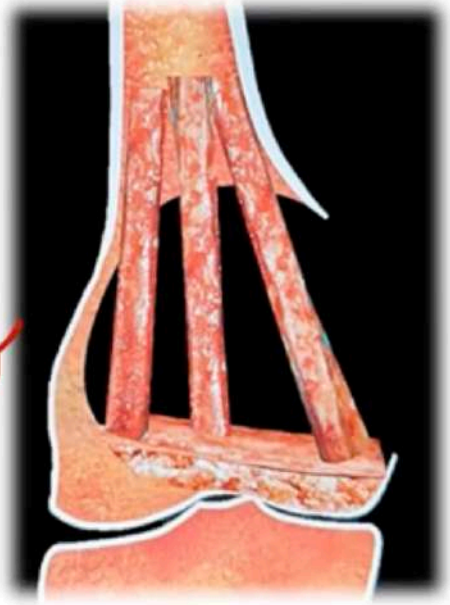
≈ PHENOL
- Penetration <1mm

≈ ARGON BEAM
- Penetration 4mm

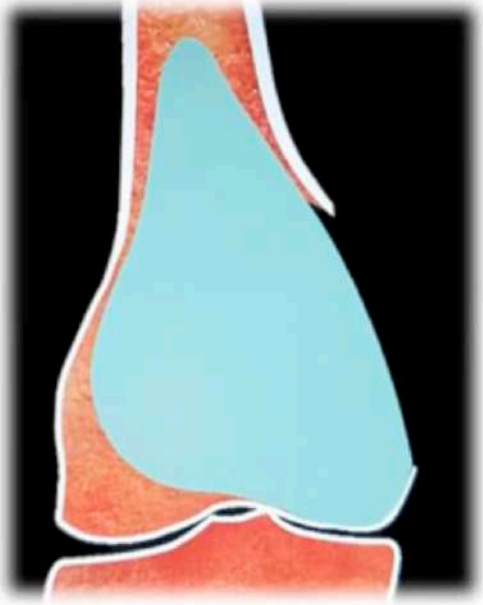
≈ HYDROGEN PEROXIDE
- Kills tumour cells by direct contact

GIANT CELL TUMOUR

BONE GRAFT



CEMENT



- BIOLOGICAL
- AVAILABILITY
- DONOR SITE MORBIDITY
- NON WEIGHT BEARING
- DIFFICULT TO PICK RECURRENCE

- NON BIOLOGICAL
- EARLY JOINT ARTHRITIS
- ? LESSER RATE OF LOCAL RECURRENCE

Giant-cell tumour of the knee

THE CONDITION OF THE CARTILAGE AFTER TREATMENT BY CURETTAGE AND CEMENTING

J Bone Joint Surg Br. 2007 Mar;89(3):361-5

F. Vult von Steyern,
I. Kristiansson,
K. Jonsson,
P. Mannfolk,
D. Heinegård,
A. Rydholm

From Lund University Hospital, Lund, Sweden

We reviewed nine patients at a mean period of 11 years (6 to 16) after curettage and cementing of a giant-cell tumour around the knee to determine if there were any long-term adverse effects on the cartilage. Plain radiography, MRI, delayed gadolinium-enhanced MRI of the cartilage and measurement of the serum level of cartilage oligomeric matrix protein were carried out. The functional outcome was evaluated using the Lysholm knee score.

Each patient was physically active and had returned to their previous occupation. Most participated in recreational sports or exercise.

The mean Lysholm knee score was 92 (83 to 100). Only one patient was found to have cartilage damage adjacent to the cement. This patient had a history of intra-articular fracture and local recurrence, leading to degenerative changes.

Interpretation of the data obtained from delayed gadolinium-enhanced MRI of the cartilage was difficult, with variation in the T1 values which did not correlate with the clinical or radiological findings. We did not find it helpful in the early diagnosis of degeneration of cartilage. We also found no obvious correlation between the serum cartilage oligomeric matrix protein level and the radiological and MR findings, function, time after surgery and the age of the patient.

In summary, we found no evidence that the long-term presence of cement close to the knee joint was associated with the development of degenerative osteoarthritis.

Mid-Term Outcome After Curettage with Polymethylmethacrylate for Giant Cell Tumor Around the Knee: Higher Risk of Radiographic Osteoarthritis?

The Journal of Bone & Joint Surgery · jbjs.org
Volume 95-A · Number 21 · November 6, 2013

Lizz van der Heijden, MSc, Michiel A.J. van de Sande, MD, PhD, Adriaan C. Heineken, Marta Fiocco, PhD, Rob G.H.H. Nelissen, MD, PhD, and P.D. Sander Dijkstra, MD, PhD

Background: It has been suggested that, when a patient has a giant cell tumor, subchondral bone involvement close to articular cartilage and a hyperthermic reaction from polymethylmethacrylate (PMMA) are risk factors for the development of osteoarthritis. We determined the prevalence, risk factors, and clinical relevance of osteoarthritis on radiographs after curettage and application of PMMA for the treatment of giant cell tumors around the knee.

Methods: This retrospective single-center study included fifty-three patients with giant cell tumor around the knee treated with curettage and PMMA between 1987 and 2007. The median age at the time of follow-up was forty-two years (range, twenty-three to seventy years). There were twenty-nine women. Radiographic evidence of osteoarthritis was defined, preoperatively and postoperatively, as Kellgren and Lawrence grade 3 or 4 (KL3-4). We studied the influence of age, sex, tumor-cartilage distance, subchondral bone involvement (≤3 mm of residual subchondral bone), subchondral bone-grafting, intra-articular fracture, multiple curettage procedures, and complications on progression to KL3-4. Functional outcomes and quality of life were assessed with the Short Form-36 (SF-36), Musculoskeletal Tumor Society (MSTS) score, and Knee injury and Osteoarthritis Outcome Score (KOOS).

Results: After a median duration of follow-up of eighty-six months (range, sixty to 285 months), six patients (11%) had progression to KL3, two (4%) had progression to KL4, and one had preexistent KL4. No patient underwent total knee replacement. The hazard ratio for KL3-4 was 9.0 (95% confidence interval [CI] = 2.0 to 41; p = 0.004) when >70% of the subchondral bone was affected and 4.2 (95% CI = 0.84 to 21; p = 0.081) when the tumor-cartilage distance was ≤3 mm. Age, sex, subchondral bone-grafting, intra-articular fracture, multiple curettage procedures, and complications did not affect progression to KL3-4. Patients with KL3-4 reported lower scores on the KOOS symptom subscale (58 versus 82; p = 0.01), but their scores on the other KOOS subscales, the MSTS score (21 versus 24), and the SF-36 (76 versus 81) were similar to those for the patients with KL0, 1, or 2 (KL0-2).

Conclusions: Seventeen percent of patients with giant cell tumor around the knee had radiographic findings of osteoarthritis after treatment with curettage and PMMA. A large amount of subchondral bone involvement close to articular cartilage increased the risk for osteoarthritis. The function and quality of life of the patients with KL3-4 were comparable with those for the patients with KL0-2, suggesting that radiographic findings of osteoarthritis at the time of intermediate follow-up had a modest clinical impact. Treatment with curettage and PMMA is safe for primary and recurrent giant cell tumors, even large tumors close to the joint.

Orthop Traumatol Surg Res. 2017 Nov;103(7):1075-1079. doi: 10.1016/j.otsr.2017.06.013. Epub 2017 Aug 3.

Does curettage-cement packing for treating giant cell tumors at the knee lead to osteoarthritis?

Caubère A[1], Harrosch S[2], Fioravanti M[2], Curvale G[2], Rochwerger A[2], Mattei JC[2].

⊕ Author information

Abstract

INTRODUCTION: Giant cell tumors (GCTs) make up 15 to 20% of bone-related tumors in adults. They are often found around the knee in the metaphysis and epiphysis area, contacting the joint cartilage. The aims of our study were to evaluate the presence of early knee osteoarthritis (OA) in patients with GCTs in the knee area treated by curettage-cement packing, and to evaluate whether replacing subchondral bone with acrylic cement has an effect on the functional outcomes and quality of life.

MATERIAL AND METHODS: This was a retrospective study of all patients operated between 2000 and 2010 by the same specialized surgical team. Functional outcomes and quality of life were evaluated in each patient using the Knee Injury and Osteoarthritis Outcome (KOOS), the Musculoskeletal Tumor Society Score (MSTS) and the Short Form-36 (SF-36). The presence of OA was evaluated in a full radiological work-up comparing the operated knee with the healthy contralateral knee. Knee OA was defined as grade 3 or grade 4 radiographic findings based on the Kellgren and Lawrence classification, and a significant difference between the operated and contralateral knee.

RESULTS: Nineteen patients were included in this study. The average follow-up was 120 months (range 60-180). Four patients (21%) had radiographic KL-3 and one patient (5%) had KL-4. Eight patients (42%) had recurrence of the GCT. The distance between the tumor and cartilage, and the area of the subchondral bone invaded by the tumor appeared to contribute to OA progression.

DISCUSSION: Resection of GCTs around the knee by curettage-cement packing did not have an effect on development of OA. In the four patients who developed knee OA, the tumor was located less than 3mm from the joint cartilage and took up more than 90% of the epiphysis. Based on these observations, there seems to be a strong correlation between the development of knee OA and the small quantity of subchondral bone left after curettage. The functional outcomes and quality of life were similar no matter the knee OA grade in patients. Replacing subchondral bone by cement had no effect on quality of life in this study.

LEVEL OF EVIDENCE: IV (retrospective study).

Zuo et al. World Journal of Surgical Oncology 2013, 11:156
http://www.wjso.com/content/11/1/156

WORLD JOURNAL OF SURGICAL ONCOLOGY

RESEARCH Open Access

Contemporary adjuvant polymethyl methacrylate cementation optimally limits recurrence in primary giant cell tumor of bone patients compared to bone grafting: a systematic review and meta-analysis

Dongqing Zuo†, Longpo Zheng†, Wei Sun, Dong Fu, Yingqi Hua* and Zhengdong Cai*

Clin Orthop Relat Res (2017) 475:776–783
DOI 10.1007/s11999-016-4755-x

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

SYMPOSIUM: 2015 MEETINGS OF THE MUSCULOSKELETAL TUMOR SOCIETY AND THE INTERNATIONAL SOCIETY OF LIMB SALVAGE

Supplemental Bone Grafting in Giant Cell Tumor of the Extremity Reduces Nononcologic Complications

Joseph Benevenia MD, Steven M. Rivero MD, Jeffrey Moore MD, Joseph A. Ippolito BA, Daniel A. Siegerman MD, Kathleen S. Beebe MD, Francis R. Patterson MD

Abstract

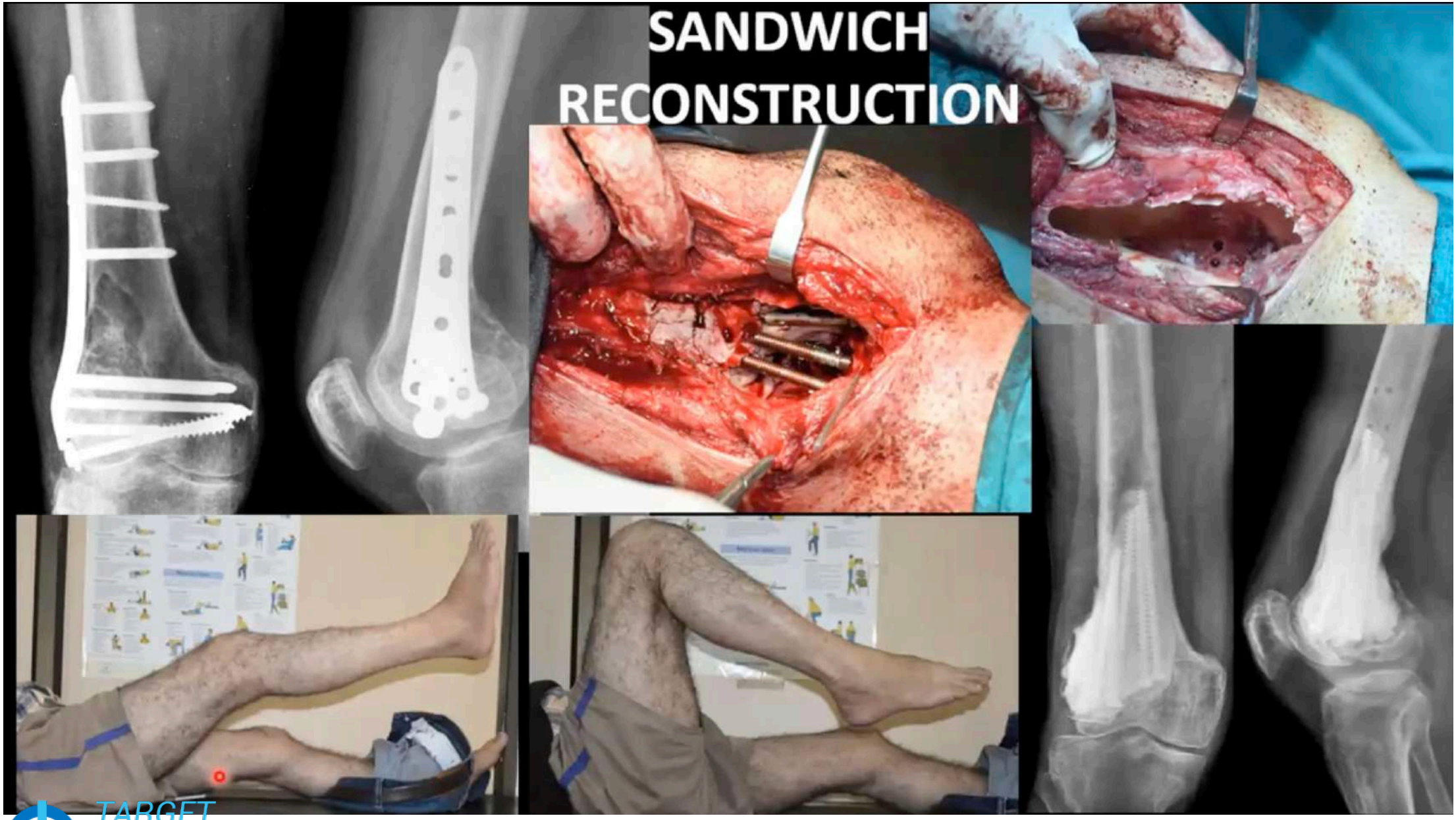
Background Giant cell tumors (GCTs) are treated with resection curettage and adjuvants followed by stabilization. Complications include recurrence, fracture, and joint degeneration. Studies have shown treatment with polymethylmethacrylate (PMMA) may increase the risk of joint degeneration and fracture. Other studies have suggested that subchondral bone grafting may reduce these risks.

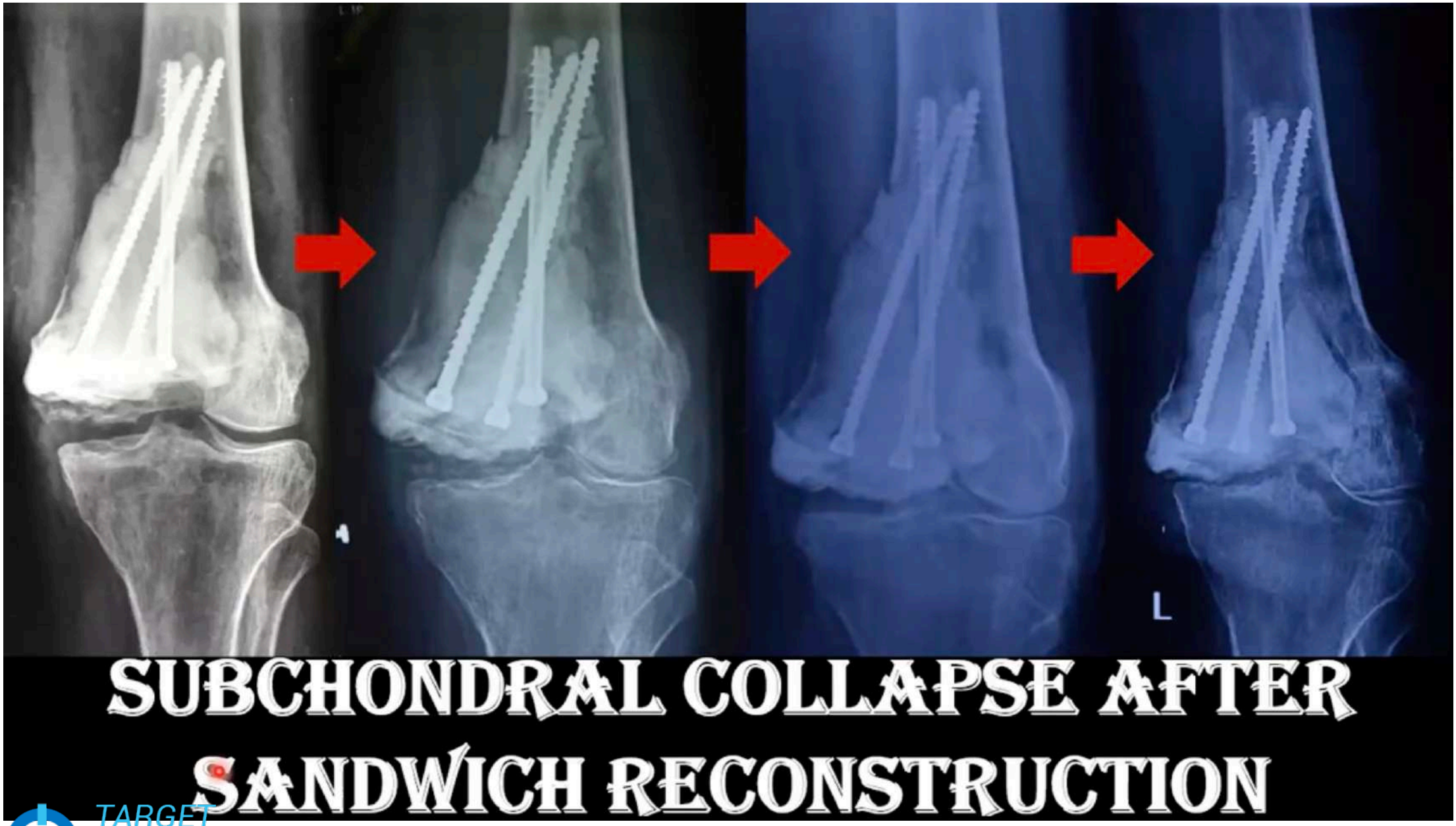
Questions/purposes Following standard intralesional resection-curettage and adjuvant treatment, is the use of bone graft, with or without supplemental PMMA, (1) associated with fewer nononcologic complications; (2) associated with differences in tumor recurrence between patients treated with versus those treated without bone grafting for GCT; and (3) associated with differences in Musculoskeletal Tumor Society (MSTS) scores?

Methods Between 1996 and 2014, 49 patients presented with GCT in the epiphysis of a long bone. Six patients were excluded, four who were lost to followup before 12 months and two because they presented with displaced, comminuted, intraarticular pathologic fractures with a nonreconstructable joint surface. The remaining 43 patients were included in our study at a mean followup of 59 months (range, 12–234 months). After resection-curettage, 21 patients were reconstructed using femoral head allograft with or without PMMA (JB) and 22 patients were reconstructed using PMMA alone (FRP, KSB); each surgeon used the same approach (that is, bone graft or no bone graft) throughout the period of study. The primary study comparison was between patients treated with bone graft (with or without PMMA) and those treated without bone graft.

Results Nononcologic complications occurred less frequently in patients treated with bone graft than those treated without (10% [two of 21] versus 55% [12 of 22]; odds ratio, 0.088; 95% confidence interval [CI], 0.02–0.47; p = 0.002). Patients with bone graft had increased nononcologic complication-free survival (hazard ratio, 4.59; 95% CI, 1.39–15.12; p = 0.012). With the numbers available, there was no difference in tumor recurrence between patients treated with bone graft versus without (29% [six of 21] versus 32% [seven of 22]; odds ratio, 0.70; 95% CI, 0.1936–2.531; p = 0.586) or in recurrence-free survival among patients with bone graft versus without (hazard ratio, 0.94; 95% CI, 0.30–2.98; p = 0.920). With the numbers available, there was no difference in mean MSTS scores between patients treated with bone graft versus without (92% ± 2% versus 93% ± 1.4%; mean difference 1.0%; 95% CI, −3.9% to 6.0%; p = 0.675).

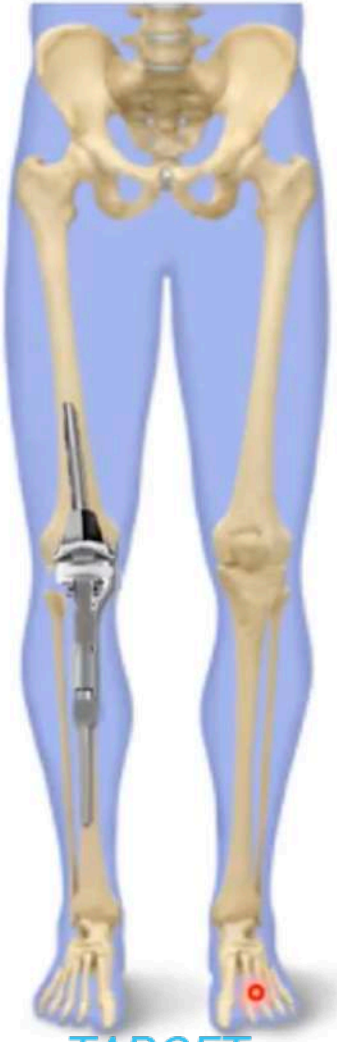
Conclusions Compared with PMMA alone, the use of periarticular bone graft constructs reduces postoperative complications apparently without increasing the likelihood of tumor recurrence.





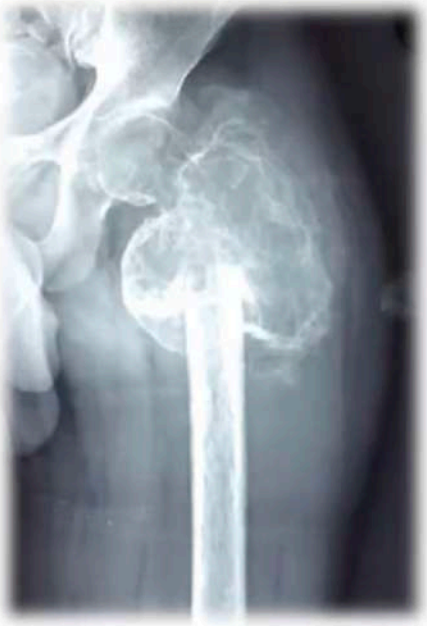
SUBCHONDRAL COLLAPSE AFTER SANDWICH RECONSTRUCTION

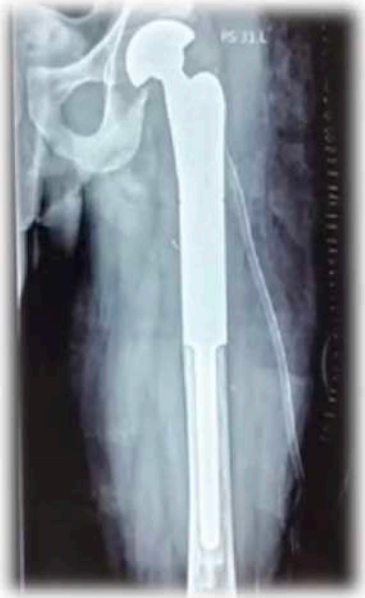
GIANT CELL TUMOUR



RESECTION

- PATHOLOGICAL FRACTURE WITH BONE DEFORMITY





CLINICAL ORTHOPAEDICS AND RELATED RESEARCH
Number 459, pp. 96–104

Joint Salvage for Pathologic Fracture of Giant Cell Tumor of the Lower Extremity

Benjamin M. Deheshi, MD, FRCSC; Shabana N. Jaffer, BSc; Anthony M. Griffin, MSc; Peter C. Ferguson, MD, MSc, FRCSC; Robert S. Bell, MD, MSc, FRCSC; and Jay S. Wunder, MD, MSc, FRCSC

Pathologic fracture through giant cell tumor is thought to be associated with higher rates of recurrence and poor functional outcome. We compared patients with and without pathologic fracture through giant cell tumor of weightbearing long bones. We retrospectively reviewed 139 patients with giant cell tumor of weightbearing long bones with (n = 43) and without (n = 96) pathologic fracture at presentation; the two groups had similar demographics. Joint salvage was successful in 84% of the fracture group and 96% of the nonfracture group. Five-year recurrence-free survival rates were comparable between the two groups (82.6% [95% confidence interval, 69.1–95.9%] in the fracture group and 77.9% [95% confidence interval, 67.7–88.1%] in the nonfracture group). There was a trend toward lower 5-year metastatic-free survival in the fracture group (94.7% [95% confidence interval, 87.3–100%]) than in the nonfracture group (97.3% [95% confidence interval, 93.5–100%]). Functional outcome was good and similar in the two groups. Arthrofibrosis was more common in the group with pathologic fracture. Joint salvage for patients with pathologic fractures through giant cell tumor of weightbearing bones is a reasonable option with functional outcomes and recurrence rates comparable to those of patients without fracture.

Giant cell tumor (GCT) of bone is a benign, locally aggressive tumor that usually involves the metaphyseal-epiphyseal region of long bones. It accounts for 5% of all primary bone tumors and 20% of all benign bone tumors.[4,14,24,32–34] There is no gender predilection, and tumors usually occur in adults 20 to 40 years old.[4,6,34] Most GCTs occur around the knee (distal femur and proximal tibia); the distal radius, sacrum, and proximal femur are other common sites.[34]

Although the majority of GCTs appear benign histologically, there is a risk of local recurrence and the potential for metastatic spread.[3,4,6,11,13,22,24,31,33,34] The standard treatment for GCTs arising adjacent to joints involves thorough intralesional curettage.[3,4,34] The rate of local control after intralesional curettage has improved with advances in surgical technique and increased awareness of the aggressive nature of the tumor.[3,4,24,29,33–36] The additional benefit of adjuvants such as phenol, cryotherapy, and cement is controversial.[3,25,27,29,33–35] The Canadian Sarcoma Group demonstrated similar local recurrence rates with use of bone graft or cement after intralesional treatment of GCTs.[3,33]

THE BONE & JOINT JOURNAL

■ ONCOLOGY

Does pathological fracture affect the rate of local recurrence in patients with a giant cell tumour of bone?

A META-ANALYSIS

A. A. Salunke,
Y. Chen,
X. Chen,
J. H. Tan,
G. Singh,
B. C. Tai,
L. W. Khin,
M. E. Puhaindran

From Department of Orthopaedic Surgery, National University Health System, Singapore

A. A. Salunke, MBBS, DNB(Orth), Clinical Fellow, Division of Musculoskeletal Oncology
Y. Chen, MBBS, MRCS (Ireland), Senior Resident, Division of Musculoskeletal Oncology
X. Chen, MD, Medical Officer,

We investigated whether the presence of a pathological fracture increased the risk of local recurrence in patients with a giant cell tumour (GCT) of bone. We also assessed if curettage is still an appropriate form of treatment in the presence of a pathological fracture. We conducted a comprehensive review and meta-analysis of papers which reported outcomes in patients with a GCT with and without a pathological fracture at presentation. We computed the odds ratio (OR) of local recurrence in those with and without a pathological fracture.

We selected 19 eligible papers for final analysis. This included 3215 patients, of whom 580 (18.0%) had a pathological fracture. The pooled OR for local recurrence between patients with and without a pathological fracture was 1.05 (95% confidence interval (CI) 0.66 to 1.67, p = 0.854). Amongst the subgroup of patients who were treated with curettage, the pooled OR for local recurrence was 1.23 (95% CI 0.75 to 2.01, p = 0.417).

A *post hoc* sample size calculation showed adequate power for both comparisons.

There is no difference in local recurrence rates between patients who have a GCT of bone with and without a pathological fracture at the time of presentation. The presence of a pathological fracture should not preclude the decision to perform curettage as carefully selected patients who undergo curettage can have similar outcomes in terms of local recurrence to those without such a fracture.

Cite this article: *Bone Joint J* 2015;97-B:1566–71.

Clin Orthop Relat Res (2013) 471:820–829
DOI 10.1007/s11999-012-2546-6

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

Giant Cell Tumor With Pathologic Fracture: Should We Curette or Resect?

Lizz van der Heijden MSc, P. D. Sander Dijkstra MD, PhD,
Domenico A. Campanacci MD, PhD,
C. L. Max H. Gibbons MD, PhD, Michiel A. J. van de Sande MD, PhD

Abstract

Background Approximately one in five patients with giant cell tumor of bone presents with a pathologic fracture. However, recurrence rates after resection or curettage differ substantially in the literature and it is unclear when curettage is reasonable after fracture.

Questions/Purposes We therefore determined: (1) local recurrence rates after curettage with adjuvants or en bloc resection; (2) complication rates after both surgical techniques and whether fracture healing occurred after curettage with adjuvants; and (3) function after both treatment modalities for giant cell tumor of bone with a pathologic fracture.

Methods We retrospectively reviewed 48 patients with fracture from among 422 patients treated between 1981 and 2009. The primary treatment was resection in 25 and curettage with adjuvants in 23 patients. Minimum followup was 27 months (mean, 101 months; range, 27–293 months).

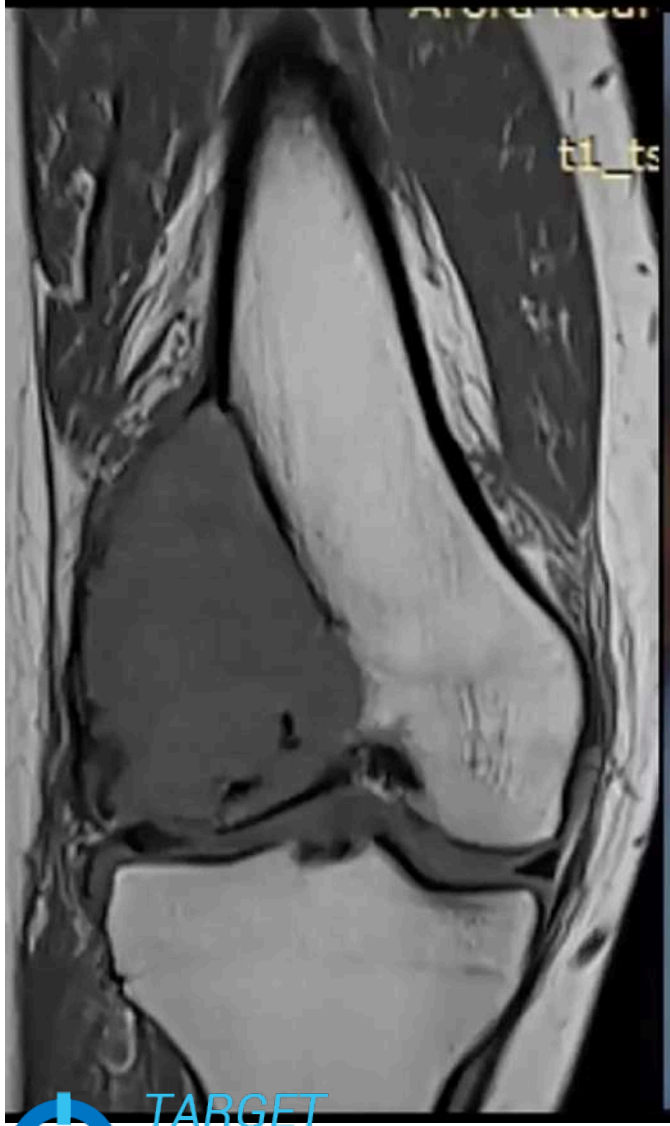
Results Recurrence rate was higher after curettage with adjuvants when compared with resection (30% versus 0%). Recurrence risk appears higher with soft tissue extension. The complication rate was lower after curettage with adjuvants when compared with resection (4% versus 16%) and included aseptic loosening of prosthesis, allograft failure, and pseudoarthrosis. Tumor and fracture characteristics did not increase complication risk. Fracture healing occurred in 24 of 25 patients. Mean Musculoskeletal Tumor Society score was higher after curettage with adjuvants (mean, 28; range, 23–30; n = 18) when compared with resection (mean, 25; range, 13–30; n = 25).

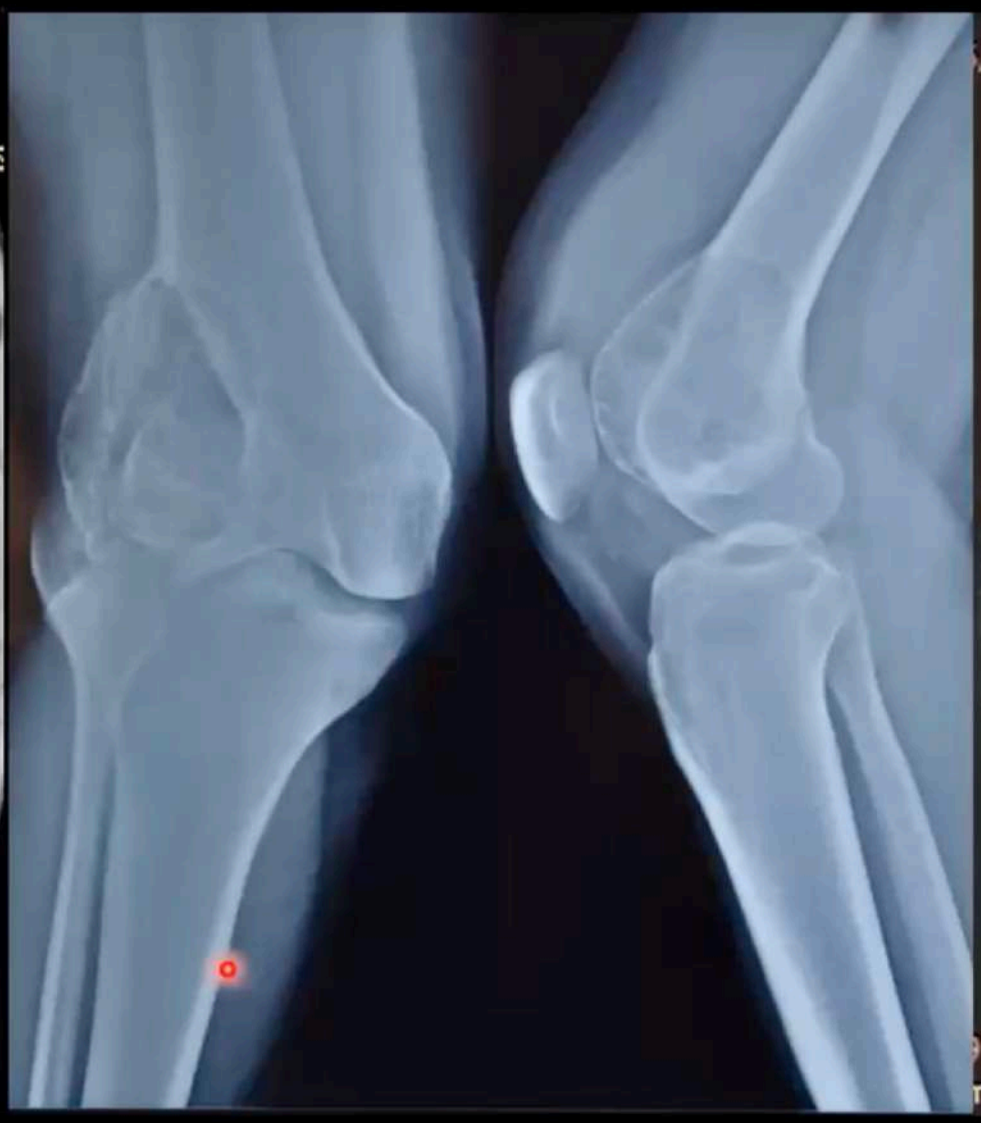
Conclusions Our observations suggest curettage with adjuvants is a reasonable option for giant cell tumor of bone with pathologic fractures. Resection should be considered with soft tissue extension, fracture through a local recurrence, or when structural integrity cannot be regained after reconstruction.

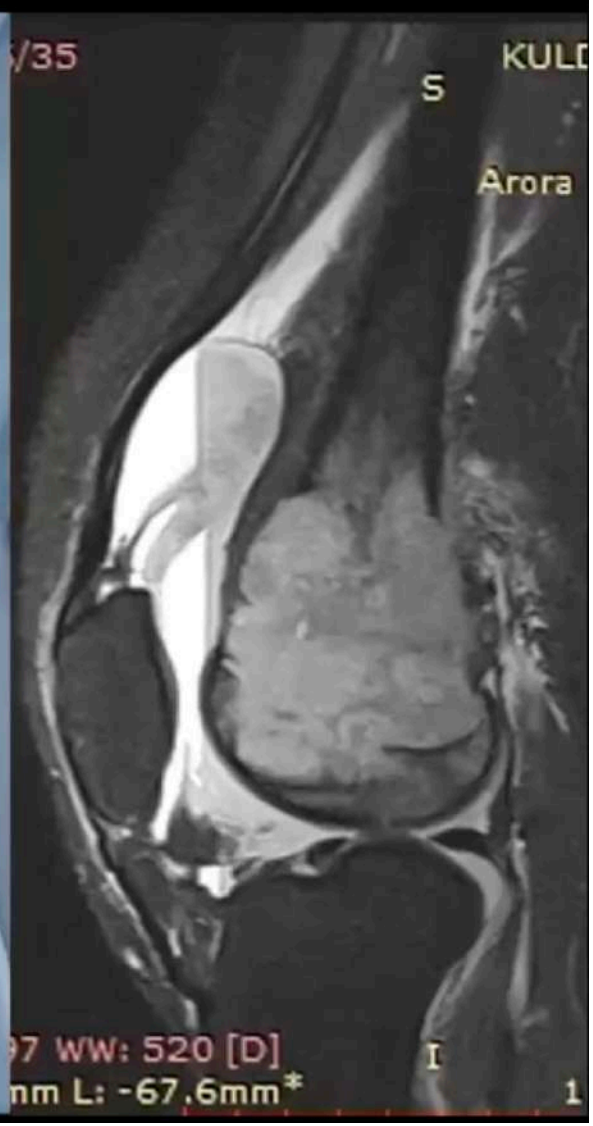
Each author certifies that he or she, or a member of his or her immediate family, has no funding or commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.
All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research* editors and board members are on file with the publication and can be viewed on request.
Each author certifies that his or her institution approved or waived approval for the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research.
This work was performed at the Leiden University Medical Center, Leiden, The Netherlands.

L. van der Heijden (✉), P. D. S. Dijkstra, M. A. J. van de Sande
Department of Orthopaedic Surgery, Leiden
University Medical Center, Postzone J11-R70,

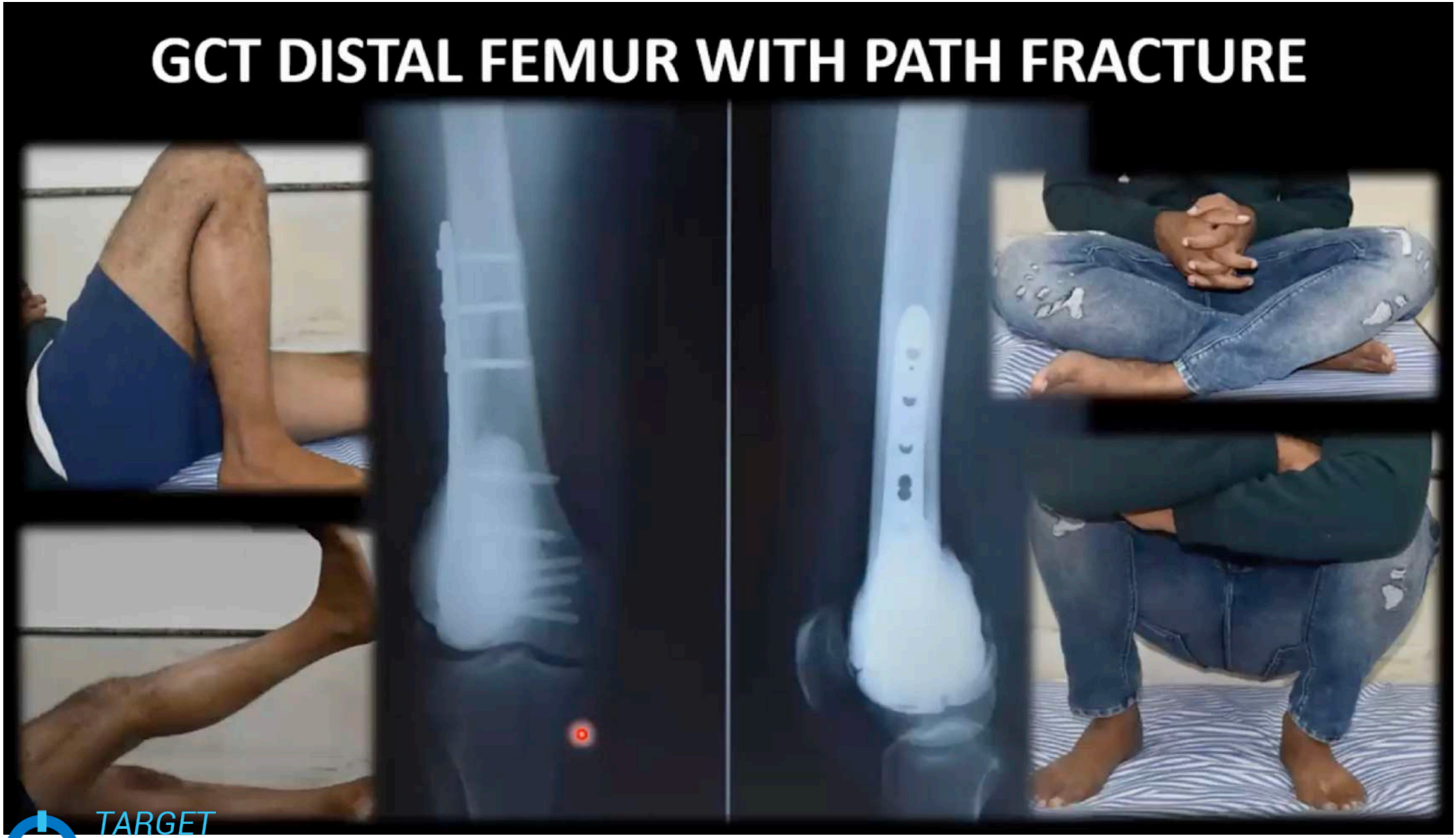
GCT DISTAL FEMUR WITH PATH FRACTURE



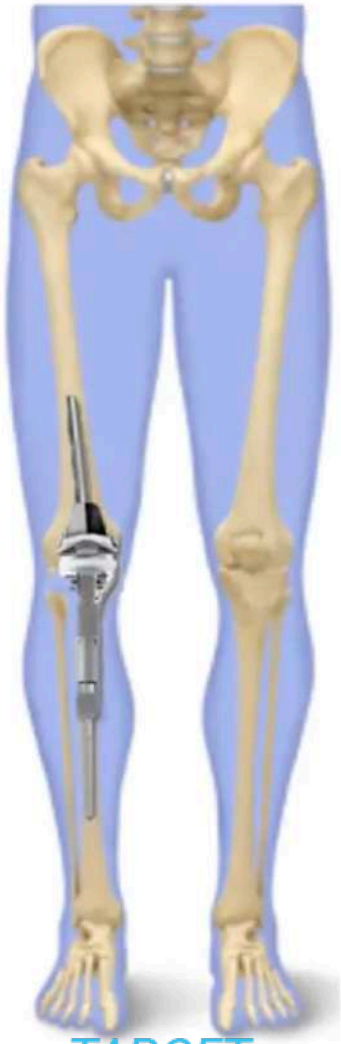




GCT DISTAL FEMUR WITH PATH FRACTURE

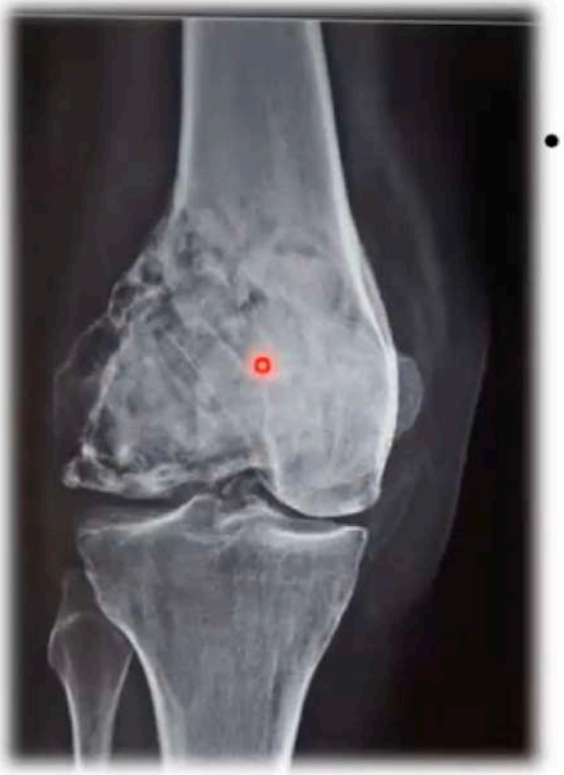


GIANT CELL TUMOUR

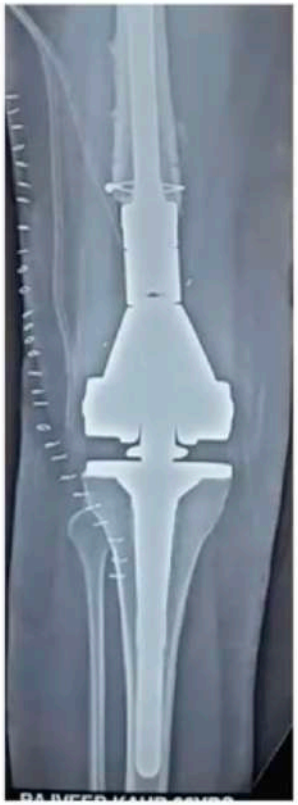


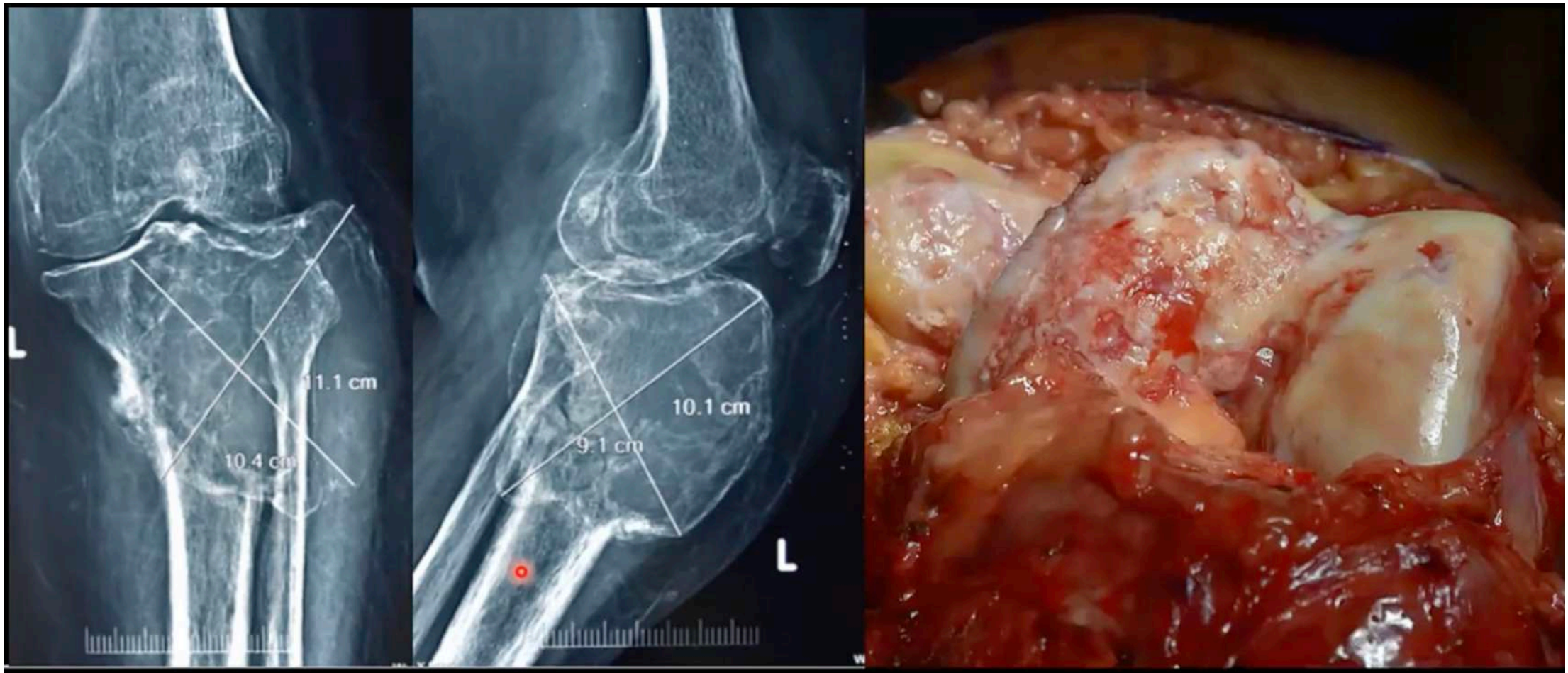
RESECTION

- PATHOLOGICAL FRACTURE WITH BONE DEFORMITY



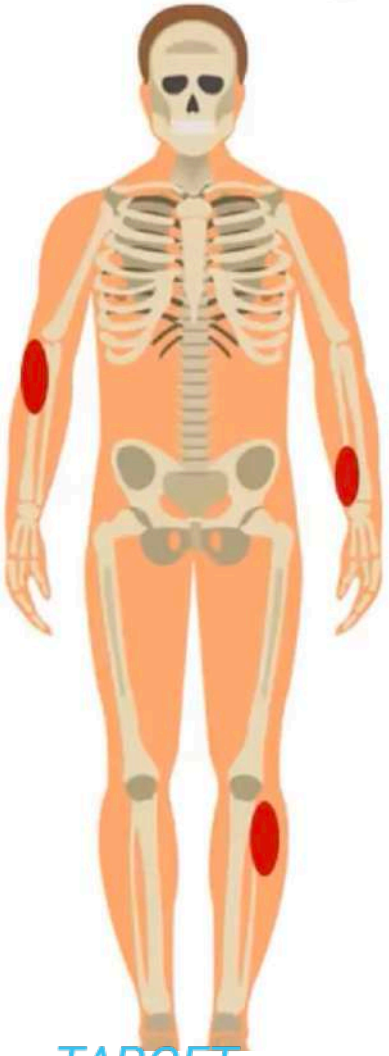
- RECURRENT CASE WITH JOINT DAMAGE OR NO RESIDUAL BONE





RECONSTRUCTION WITH MEGAPROSTHESIS

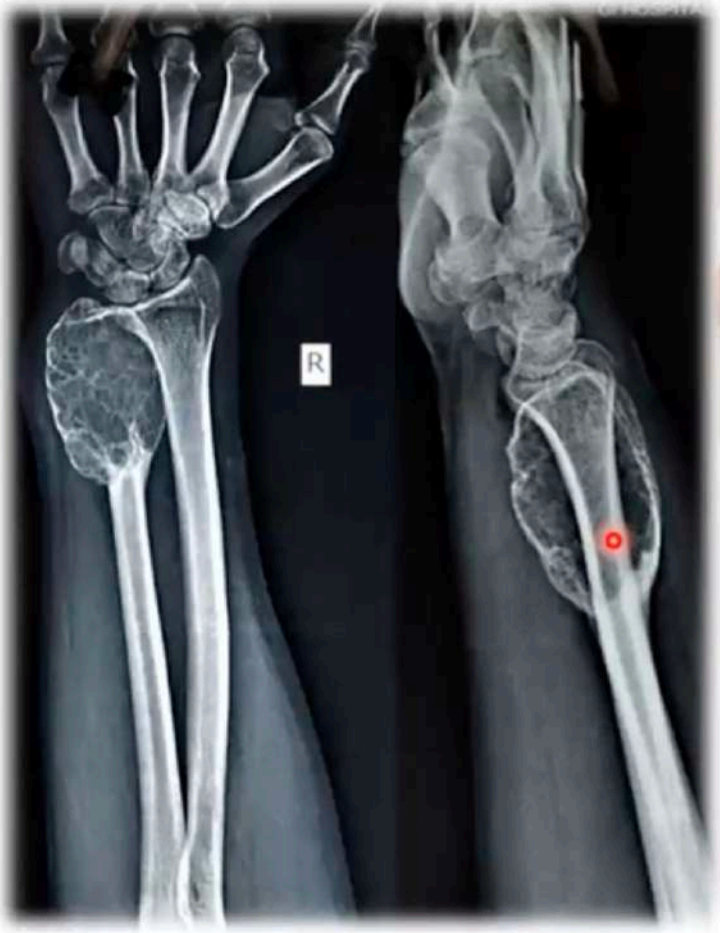
GIANT CELL TUMOUR

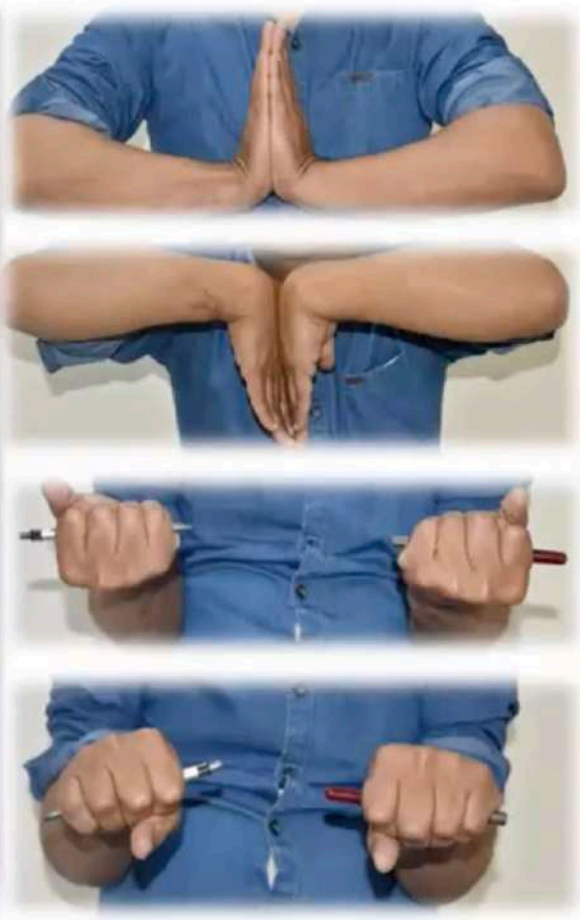


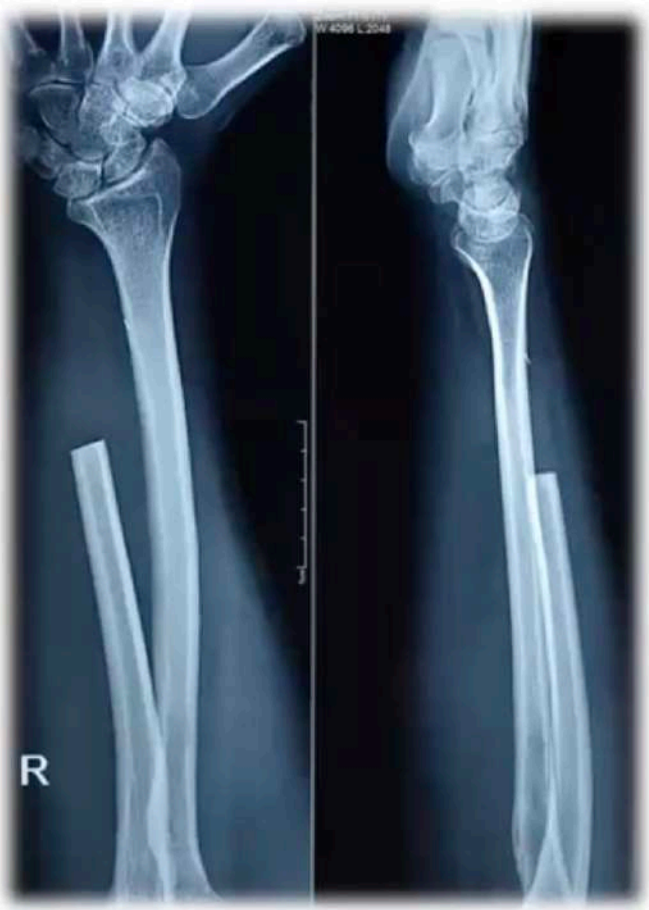
RESECTION

- PATHOLOGICAL FRACTURE WITH BONE DEFORMITY
- RECURRENT CASE WITH JOINT DAMAGE OR NO RESIDUAL BONE
- EXPENDABLE BONES

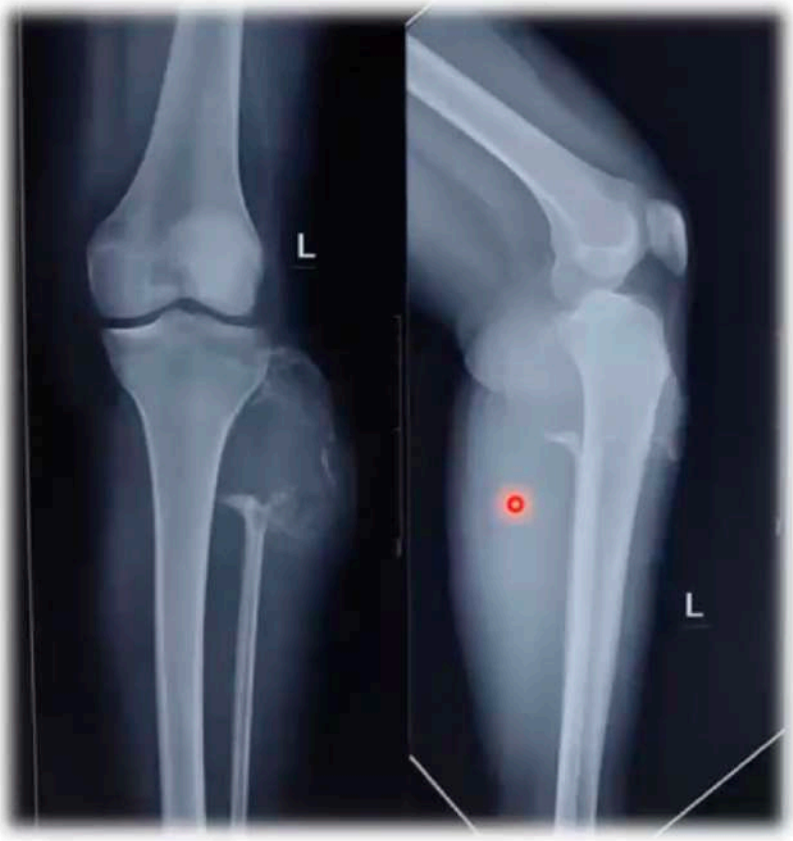
GIANT CELL TUMOUR

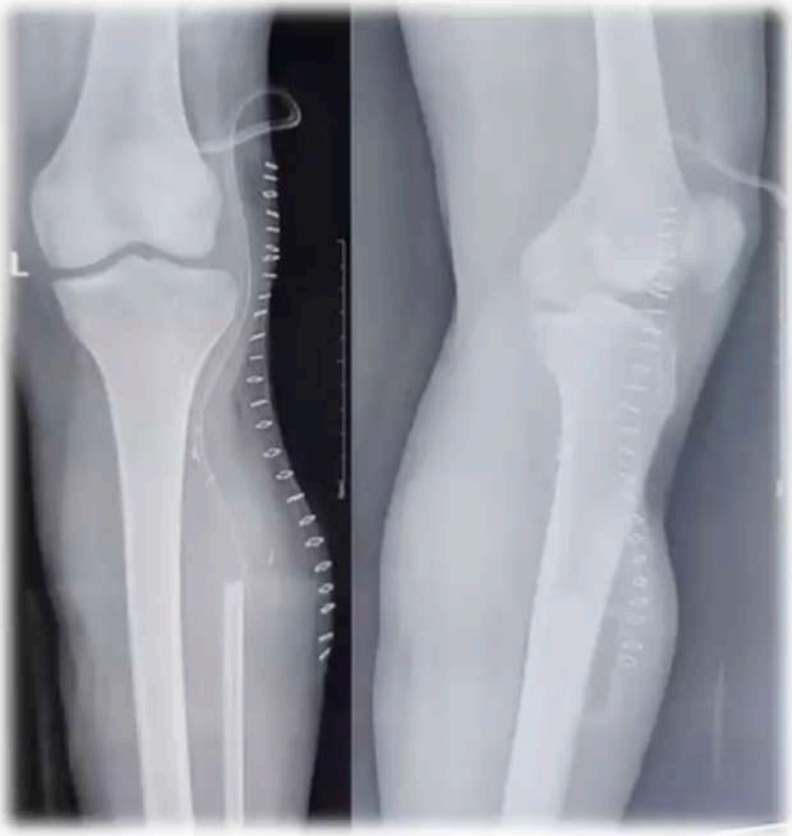






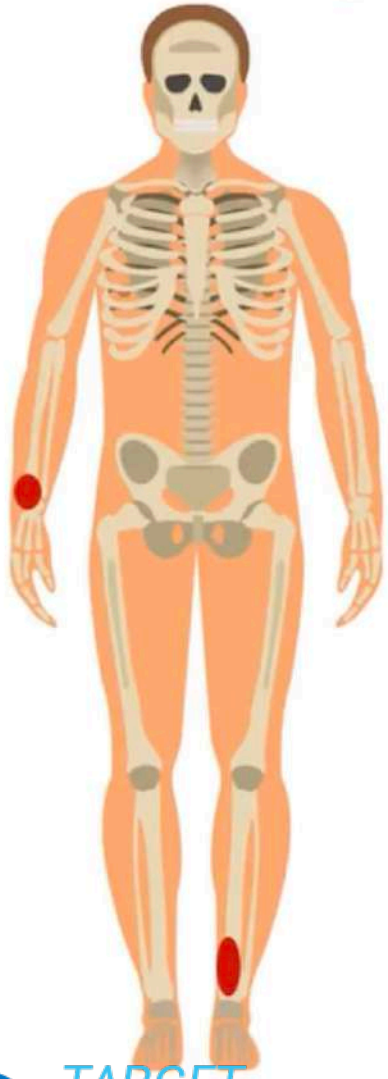
GIANT CELL TUMOUR





GIANT CELL TUMOUR

RESECTION



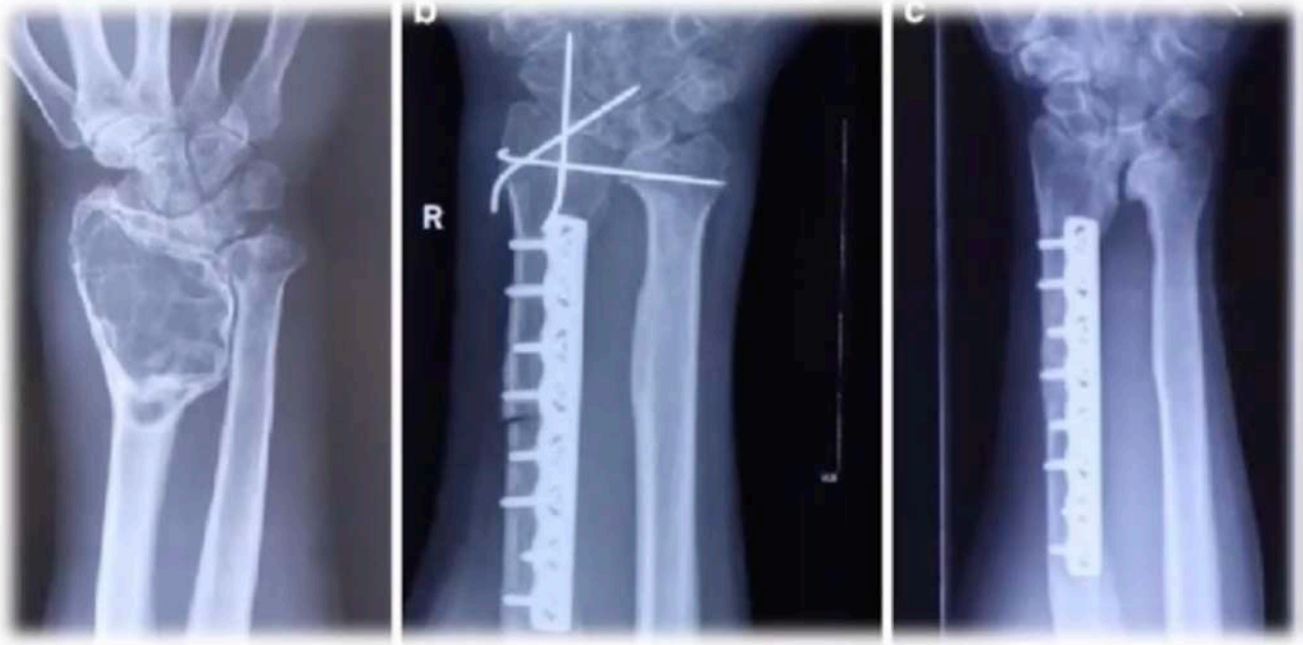
RECONSTRUCTION IS PREFERRED WITH BONE

GIANT CELL TUMOUR

DISTAL RADIUS

FIBULA ARTHROPLASTY

- WRIST MOVEMENTS
- BETTER COSMESIS



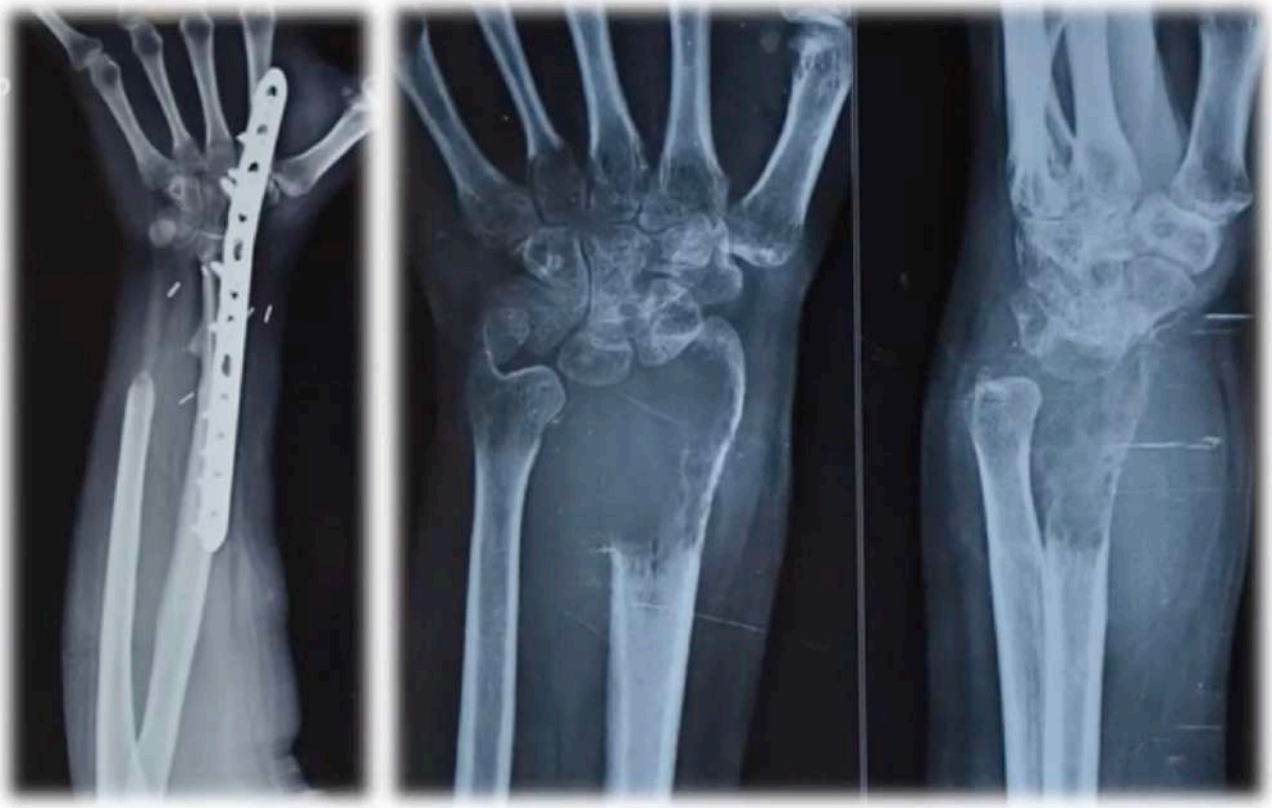
- UNSTABLE JOINT
- DONOR SITE MORBIDITY
- AVASCULAR GRAFT
- JOINT INCONGRUENCY

GIANT CELL TUMOUR

DISTAL RADIUS

ULNAR TRANSLOCATION

- STABLE JOINT
- VASCULAR GRAFT
- NO DONOR SITE MORBIDITY
- FULL PRONATION SUPINATION



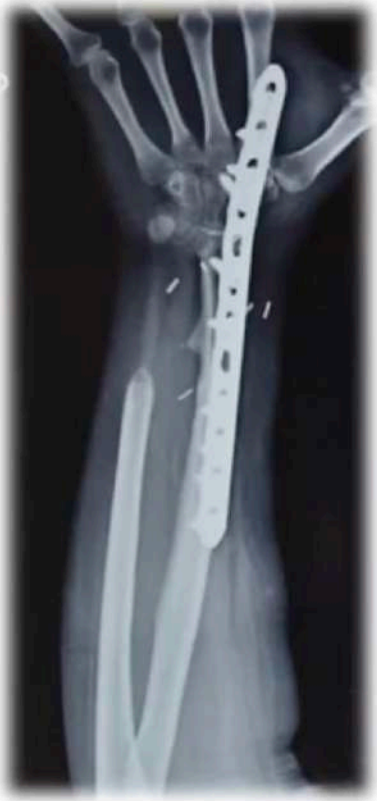
GIANT CELL TUMOUR

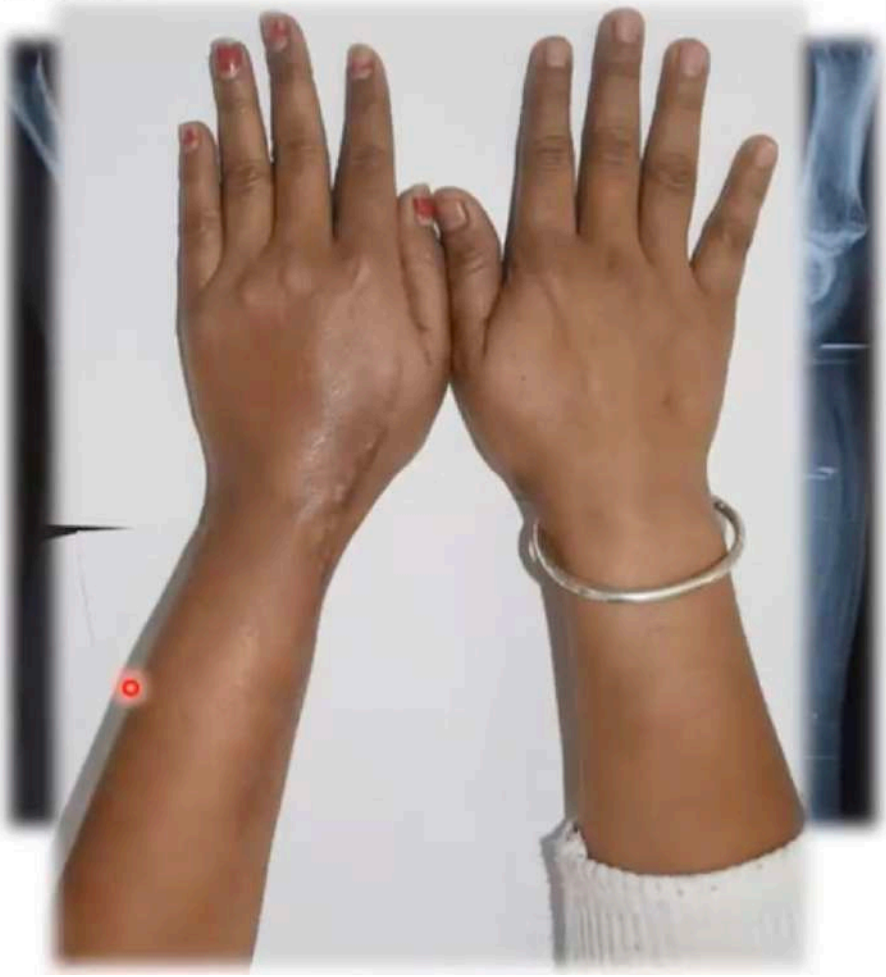
DISTAL RADIUS

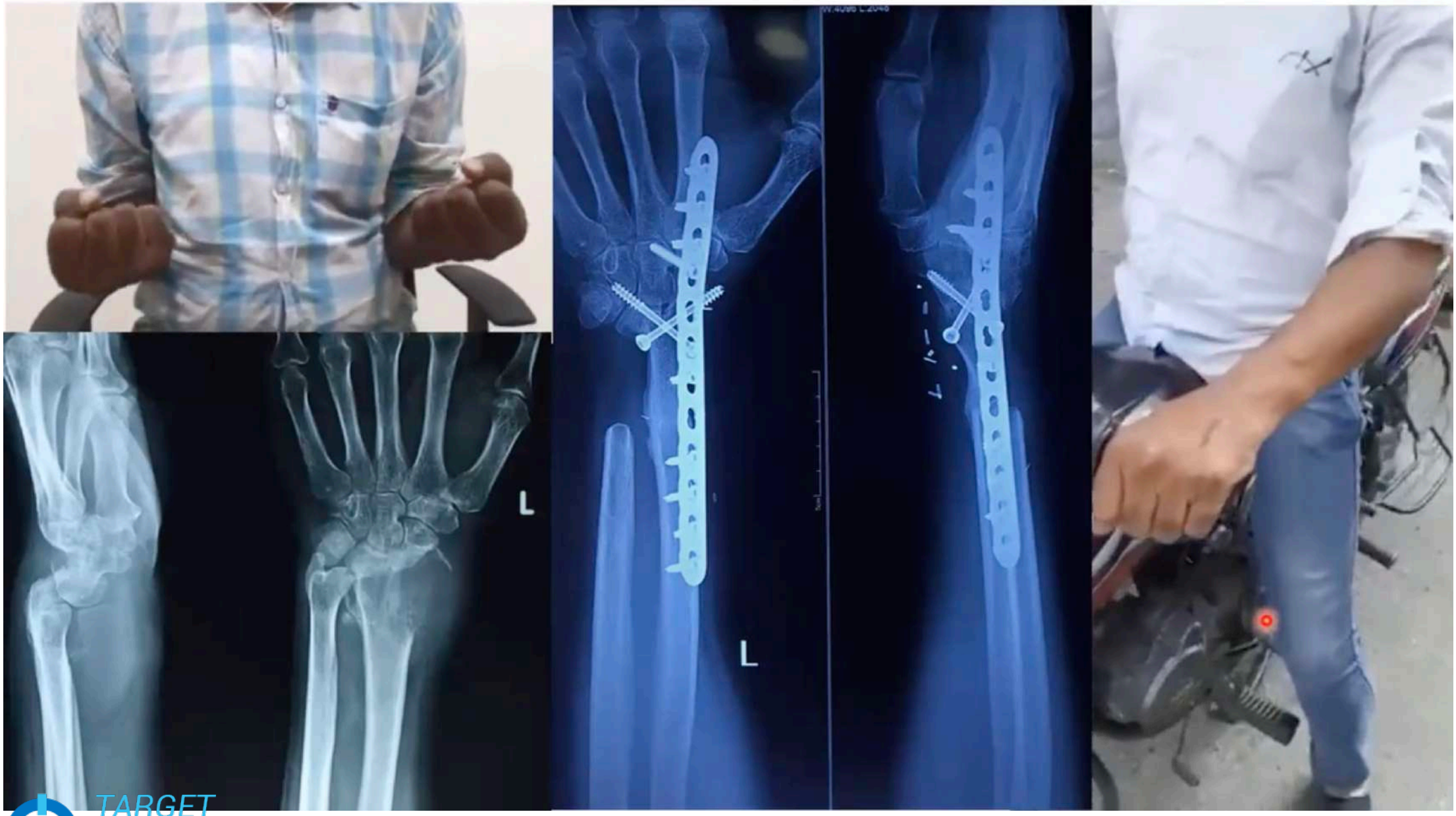
ULNAR TRANSLOCATION

- STABLE JOINT
- VASCULAR GRAFT
- NO DONOR SITE MORBIDITY
- FULL PRONATION SUPINATION

- HOUR GLASS WRIST







GIANT CELL TUMOUR

TREATMENT

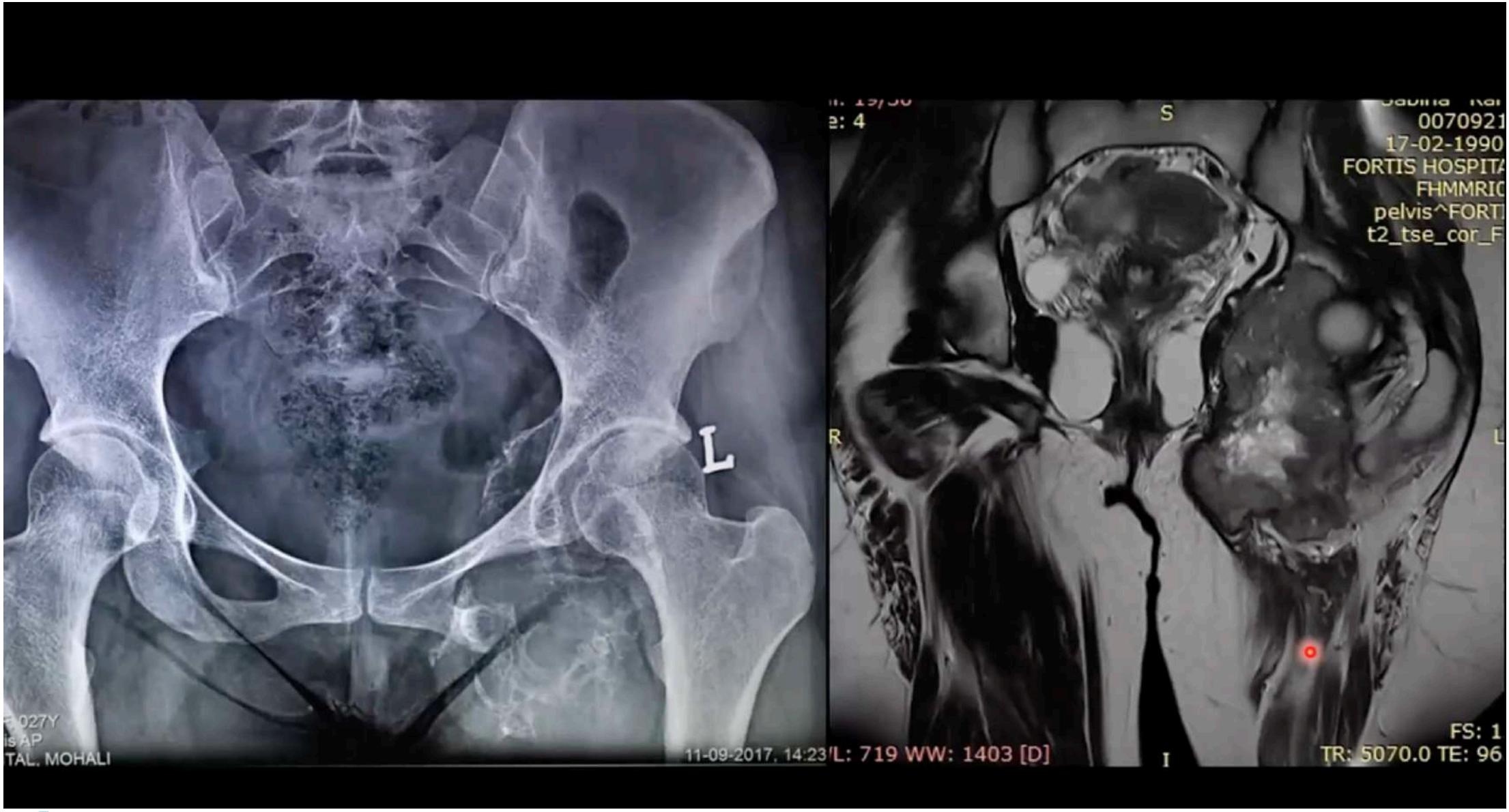
DECREASES BLOOD SUPPLY TO TUMOUR CELLS

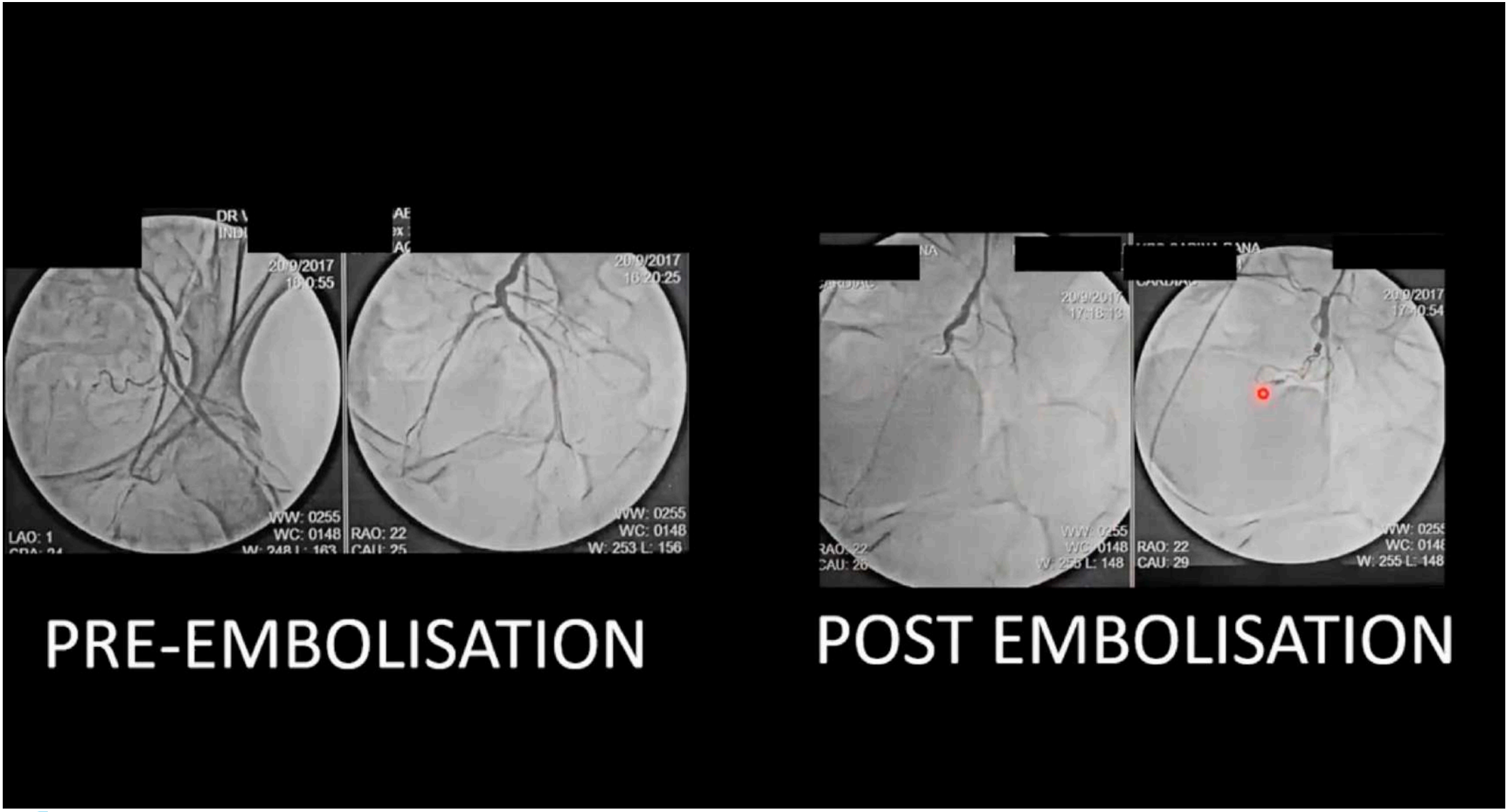
NON SURGICAL MODALITIES

- **ANGIOEMBOLISATION**

PRIOR TO CURETTAGE

DEFINITIVE TREATMENT WITH BISPHOSPHONATES IN UNRESECTABLE GCT





PRE-EMBOLISATION

POST EMBOLISATION

GIANT CELL TUMOUR

TREATMENT

CAUSE APOPTOSIS OF OSTEOCLASTS

ADJUVANT TO DECREASE RISK OF LOCAL RECURRENCE

NON SURGICAL MODALITIES

- ANGIOEMBOLISATION
- **ZOLENDRONIC ACID**

DEFINITIVE TREATMENT WITH ANGIOEMBOLISATION IN UNRESECTABLE GCT

GIANT CELL TUMOUR

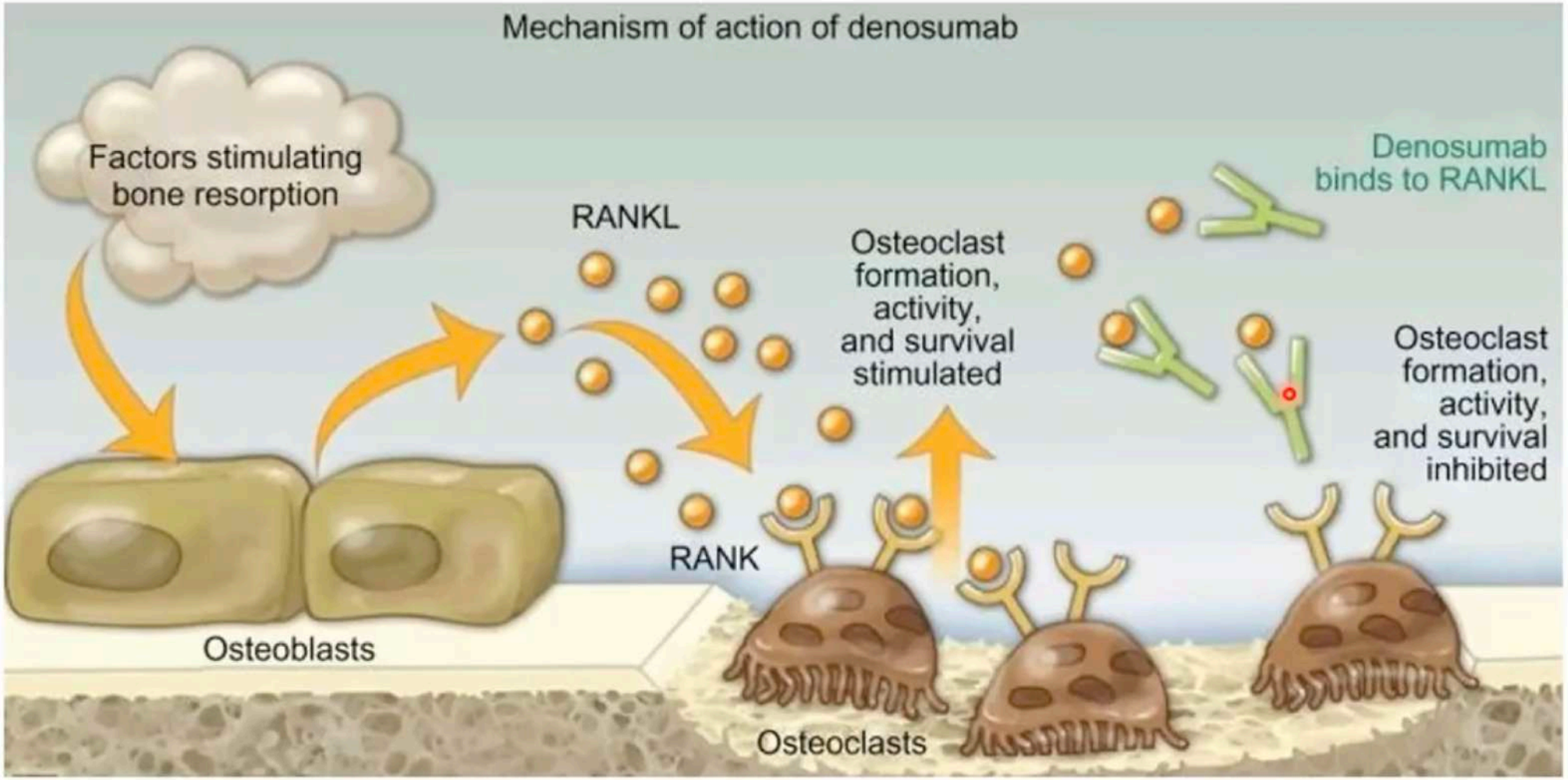
TREATMENT

MONOCLONAL ANTIBODY AGAINST RANKL

NON SURGICAL MODALITIES

- ANGIOEMBOLISATION
- ZOLENDRONIC ACID
- DENOSUMAB

GIANT CELL TUMOUR



Denosumab in patients with giant-cell tumour of bone: an open-label, phase 2 study

David Thomas, Robert Henshaw, Keith Skubitz, Sant Chawla, Arthur Staddon, Jean-Yves Blay, Martine Roudier, Judy Smith, Zhishen Ye, Winnie Sohn, Roger Dansey, Susie Jun

Summary

Background Giant-cell tumour (GCT) of bone is a primary osteolytic bone tumour with low metastatic potential and is associated with substantial skeletal morbidity. GCT is rich in osteoclast-like giant cells and contains mononuclear (stromal) cells that express RANK ligand (RANKL), a key mediator of osteoclast activation. We investigated the potential therapeutic effect of denosumab, a fully human monoclonal antibody against RANKL, on tumour-cell survival and growth in patients with GCT.

Methods In this open-label, single-group study, 37 patients with recurrent or unresectable GCT were enrolled and received subcutaneous denosumab 120 mg monthly (every 28 days), with loading doses on days 8 and 15 of month 1. The primary endpoint was tumour response, defined as elimination of at least 90% of giant cells or no radiological progression of the target lesion up to week 25. Study recruitment is closed; patient treatment and follow-up are ongoing. The study is registered with Clinical Trials.gov, NCT00396279.

Findings Two patients had insufficient histology or radiology data for efficacy assessment. 30 of 35 (86%; 95% CI 70–95) of evaluable patients had a tumour response: 20 of 20 assessed by histology and 10 of 15 assessed by radiology. Adverse events were reported in 33 of 37 patients; the most common being pain in an extremity (n=7), back pain (n=4), and headache (n=4). Five patients had grade 3–5 adverse events, only one of which (grade 3 increase in human chorionic gonadotropin concentration not related to pregnancy) was deemed to be possibly treatment related. Five serious adverse events were reported although none were deemed treatment related.

Interpretation Further investigation of denosumab as a therapy for GCT is warranted.

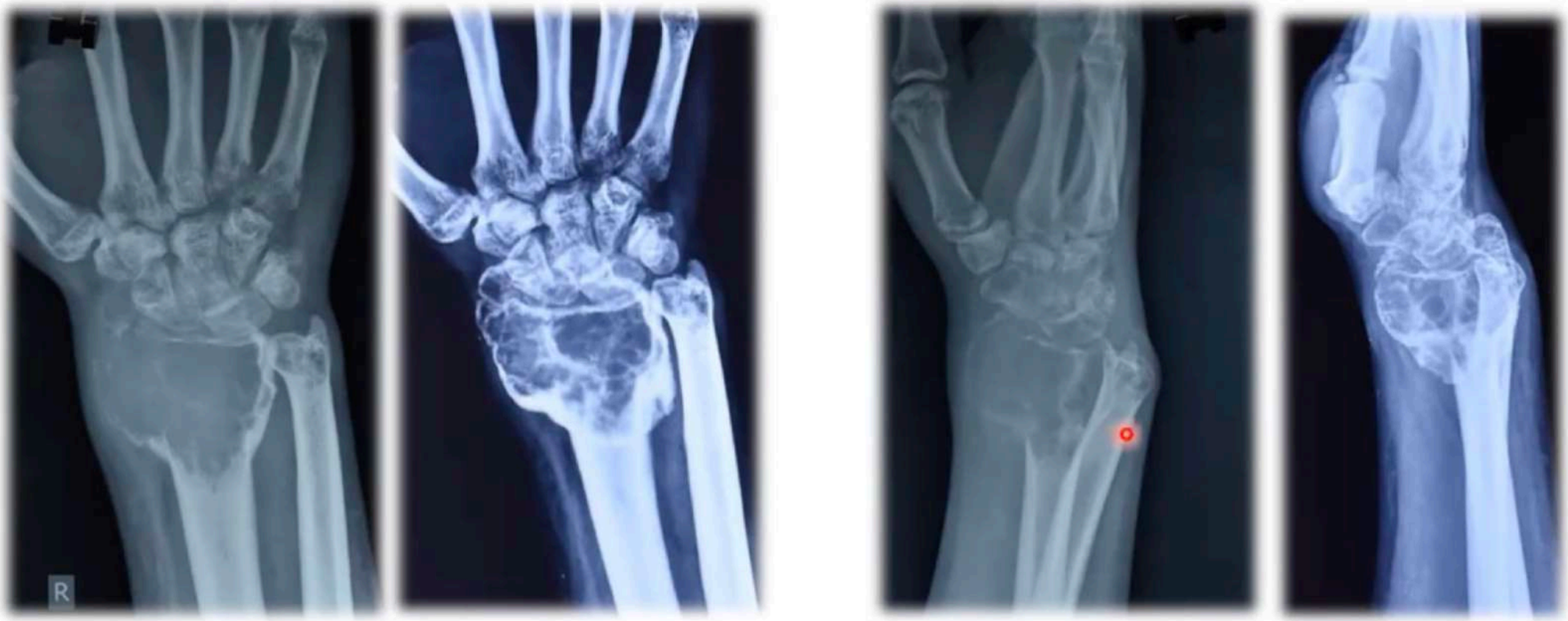
Lancet Oncol 2010; 11: 275–80

Published Online February 10, 2010 DOI:10.1016/S1470-2045(10)70010-3

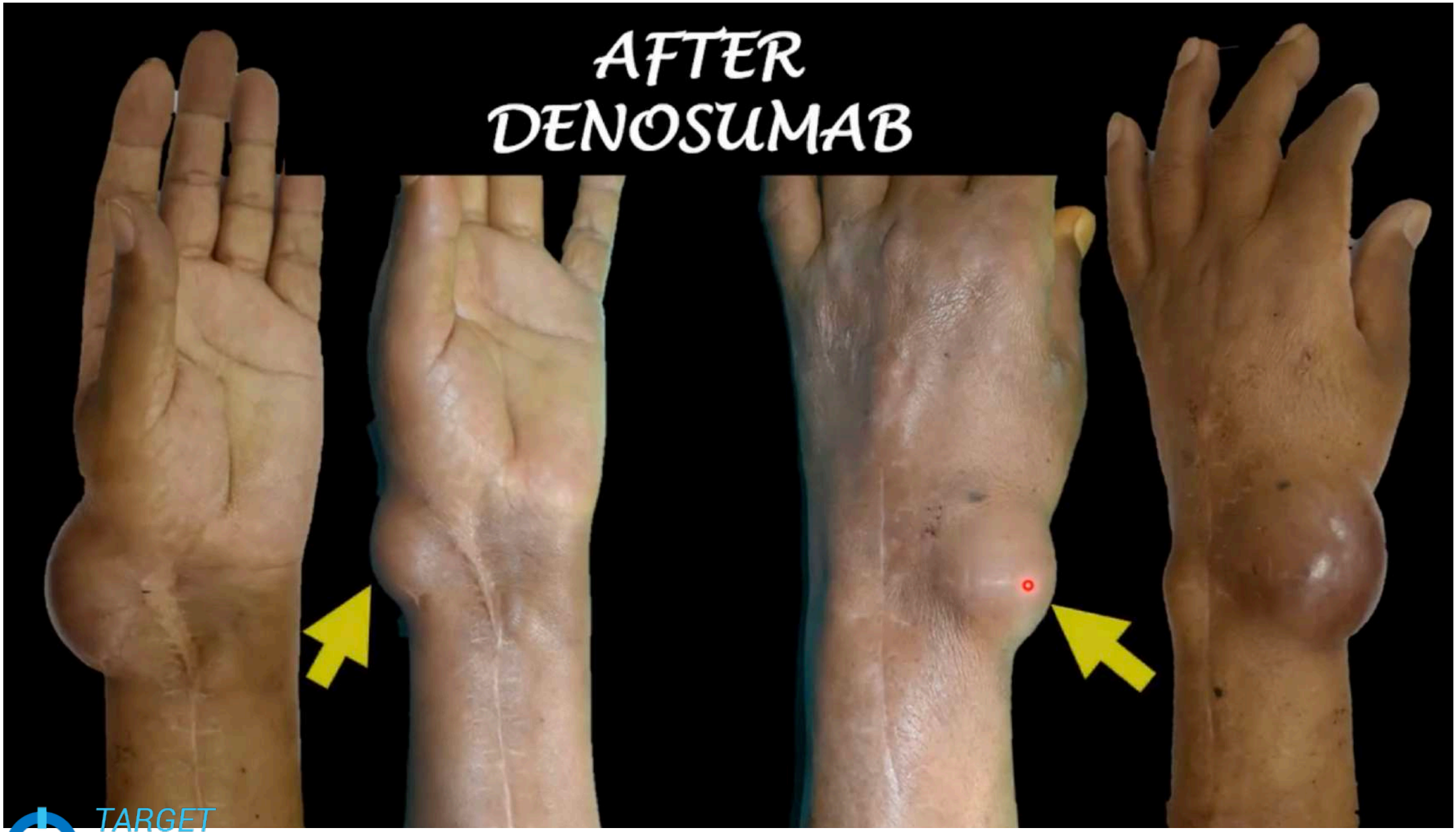
See Reflection and Reaction page 218

Peter MacCallum Cancer Centre, East Melbourne, VIC, Australia (D Thomas FRACP); Washington Cancer Institute, Georgetown University School of Medicine, Washington, DC, USA (R Henshaw MD); Division of Hematology, Oncology, and Transplantation and Masonic Cancer Center, University of Minnesota, Minneapolis, MN, USA (Prof K Skubitz MD); Sarcoma Oncology Center, Santa Monica, CA, USA (S Chawla MD); University of Pennsylvania School of Medicine, Philadelphia, PA,

GIANT CELL TUMOUR



POST DENOSUMAB



Effects of Denosumab

Pre-operative

- Significant improvement in pain after 3-4 doses

Operative

- Hardened shell - easier handling and dissection
- Reduction in vascularity - decreased blood loss

Denosumab May Increase the Risk of Local Recurrence in Patients with Giant-Cell Tumor of Bone Treated with Curettage

Costantino Errani, MD, PhD, Shinji Tsukamoto, MD, PhD, Giulio Leone, MD, Alberto Righi, MD, PhD, Manabu Akahane, MD, PhD, Yasuhito Tanaka, MD, PhD, and Davide Maria Donati, MD, PhD

Investigation performed at the Departments of Orthopaedic Oncology and Pathology, Rizzoli Institute, Bologna, Italy

Background: Recent clinical studies have suggested that denosumab is associated with tumor response and reduced surgical morbidity in patients with giant-cell tumor of bone (GCTB). We therefore evaluated the recurrence-free survival rate of patients who had GCTB in an extremity and were treated with surgery and denosumab, to determine the influence of denosumab and clinical factors on the risk of local recurrence.

Methods: We retrospectively reviewed the medical records of 408 patients treated for GCTB in an extremity in a single institution from 1990 through 2013. Two hundred and forty-seven patients underwent curettage (intralesional surgery) with a high-speed burr, and 161 underwent resection. Phenol adjuvant was used in 221 of the 247 patients who had curettage. We also reviewed the medical records of 30 patients treated surgically (25 with curettage and 5 with resection) and with denosumab from 2010 through 2013 and compared their clinical results with 378 historical control subjects. The overall minimum duration of follow-up was 24 months.

Results: The local recurrence rates were 60% (15) of 25 patients treated with curettage and denosumab and 16% (36) of 222 patients treated with curettage alone. The joint preservation rates were 80% (20) of 25 patients treated with curettage and denosumab and 94% (209) of 222 patients treated with curettage alone. Univariate and multivariable analyses showed that denosumab was the only independent factor associated with a poor prognosis when recurrence-free survival and joint preservation were considered. The overall median duration of follow-up was 85.6 months (interquartile range, 54.3 to 125.1 months). Viable tumor was present in all 30 specimens from patients treated with denosumab.

Conclusions: There was a higher rate of recurrence in the cohort exposed to denosumab. Because there were substantial differences in the cohorts and randomization was not applied, however, causation could not be evaluated.

DOI: HTTPS://DOI.ORG/10.5114/PJP.2016.65873 POL J PATHOL 2016; 67 (4): 392-397

ORIGINAL PAPER

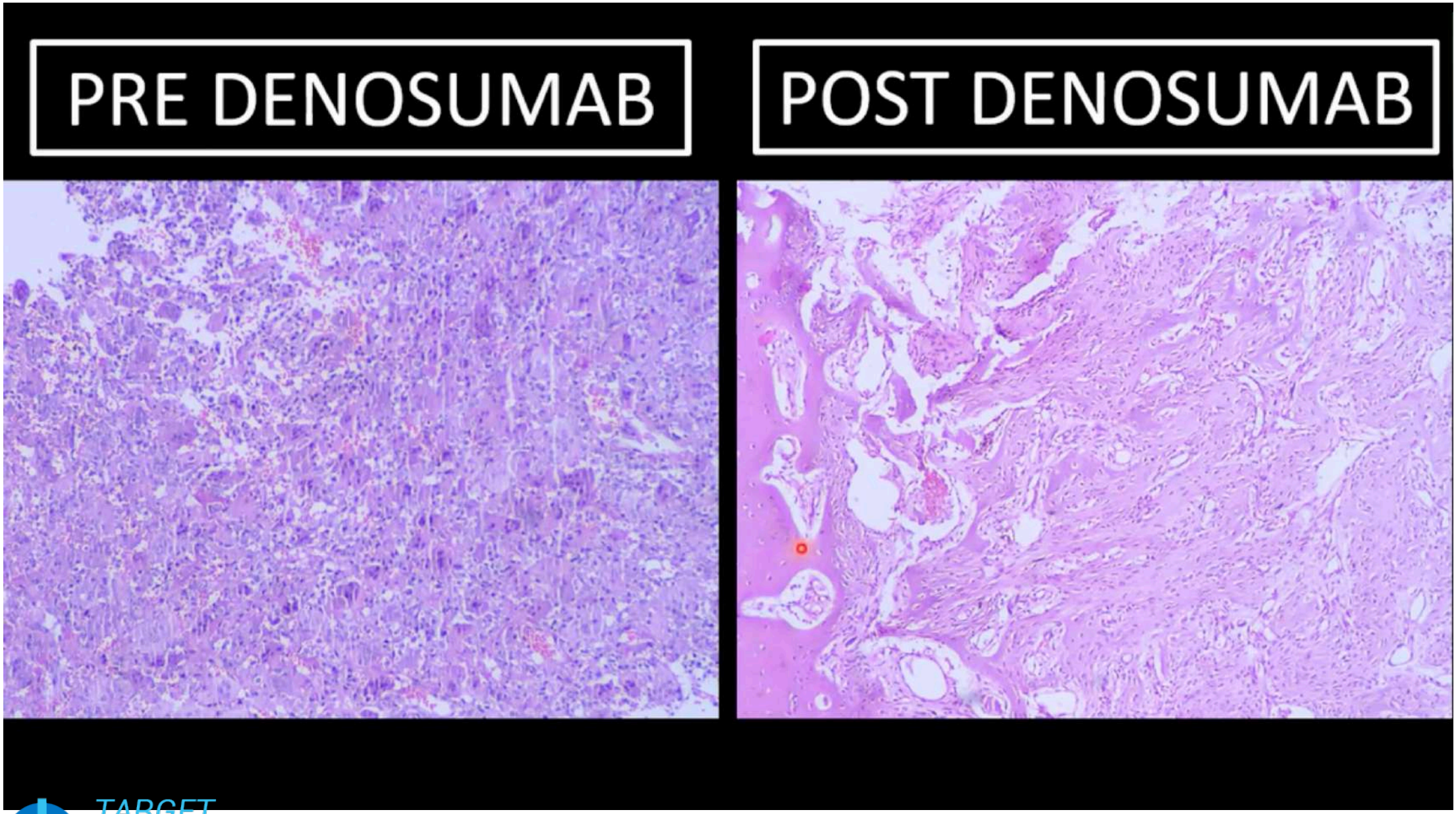
MORPHOLOGIC EVALUATION OF THE EFFECT OF DENOSUMAB ON GIANT CELL TUMORS OF BONE AND A NEW GRADING SCHEME

Pathol. Oncol. Res.
DOI 10.1007/s12253-016-0123-0

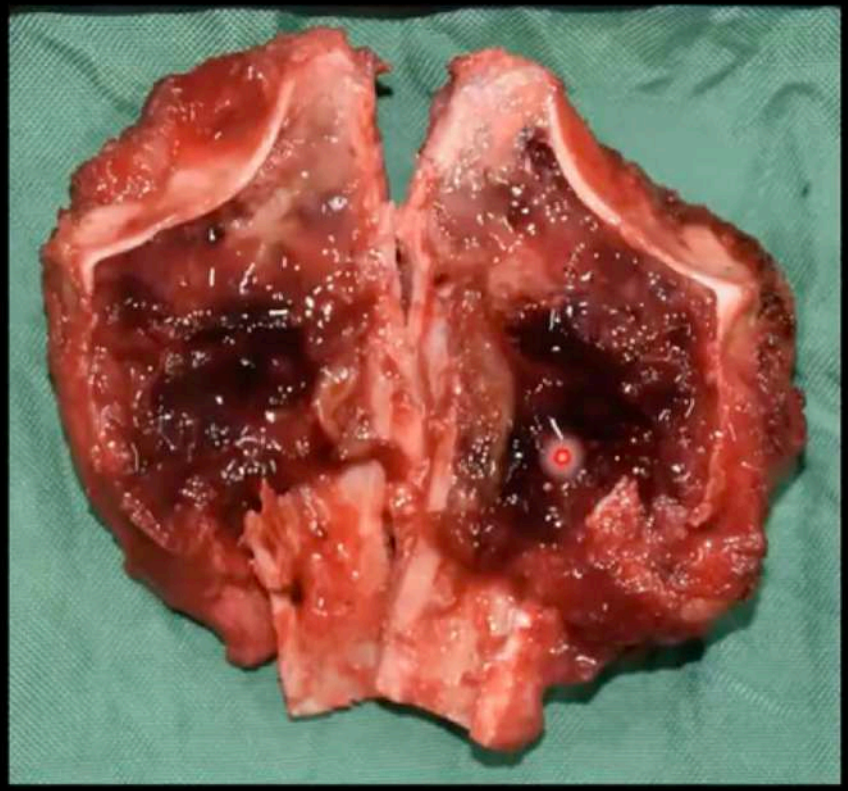
ORIGINAL ARTICLE

Clinicopathological Features of a Series of 27 Cases of Post-Denosumab Treated Giant Cell Tumors of Bones: A Single Institutional Experience at a Tertiary Cancer Referral Centre, India

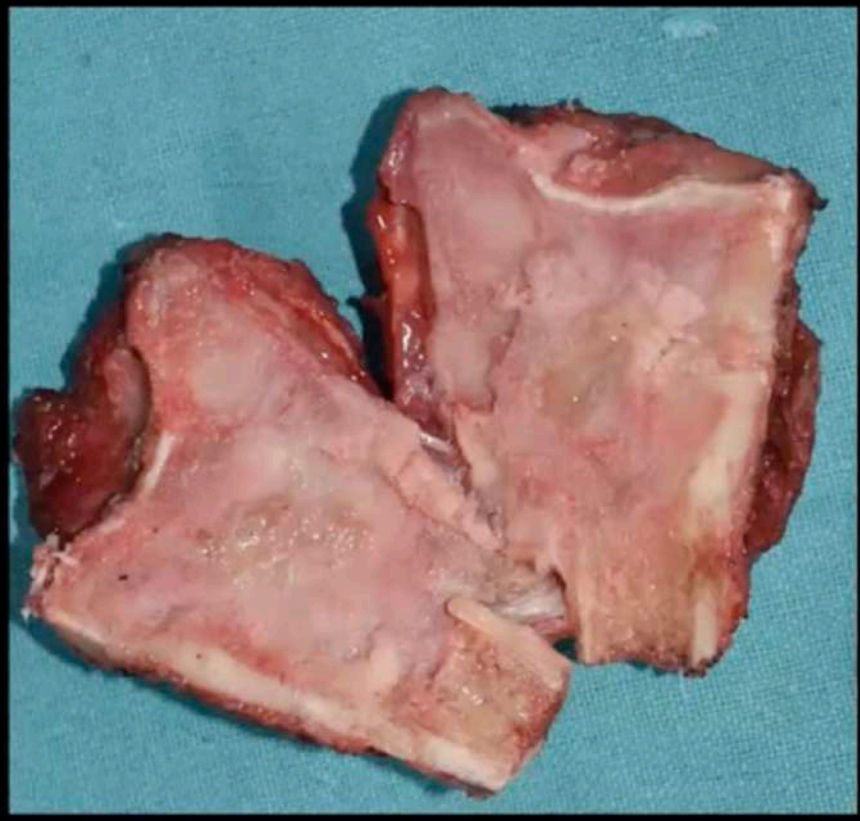
Bharat Rekhi[1] · Vivek Verma[2] · Ashish Gulia[2] · Nirmala A. Jambhekar[1] · Subhash Desai[3] · Shashikant L. Juvekar[3] · Jyoti Bajpai[4] · Ajay Puri[2]



WITHOUT DENOSUMAB



WITH DENOSUMAB



NO ROLE OF DENOSUMAB IN ADJUVANT SETTING TO DECREASE RECURRENCE

A Translational Study of the Neoplastic Cells of Giant Cell Tumor of Bone Following Neoadjuvant Denosumab

Isabella W.Y. Mak, MSc*, Nathan Evaniew, MD*, Snezana Popovic, MD, Richard Tozer, MD, and Michelle Ghert, MD

Investigation performed at the Departments of Surgery, Pathology and Molecular Science, and Oncology, McMaster University, Hamilton, and the Juravinski Cancer Centre, Hamilton Health Sciences, Hamilton, Ontario, Canada

Background: Giant cell tumor of bone is a primary bone tumor that is treated surgically and is associated with high morbidity in many cases. This tumor consists of giant cells expressing RANK (receptor activator of nuclear factor-κB) and mesenchymal spindle-like stromal cells expressing RANKL (RANK ligand); the interaction of these cells leads to bone resorption. Denosumab is a monoclonal antibody that binds RANKL and directly inhibits osteoclastogenesis. Clinical studies have suggested clinical and histological improvement when denosumab was administered to patients with a giant cell tumor. However, no studies have yet examined the viability and functional characteristics of tumor cells following denosumab treatment.

Methods: Specimens were obtained from six patients with a histologically confirmed giant cell tumor. Two of the patients had been treated with denosumab for six months. Primary cultures of stromal cells from fresh tumor tissue were established. Cell proliferation was measured over a two-day time course. The expression of RANKL and osteoprotegerin was analyzed with use of real-time PCR (polymerase chain reaction).

Results: Histological specimens from both patients who had completed denosumab treatment showed the absence of giant cells but persistence of stromal cells. Cell proliferation studies indicated that proliferation of stromal cells cultured from clinical specimens following denosumab treatment was approximately 50% slower than that of specimens from untreated patients. The expression of RANKL in the specimens from the treated patients was almost completely eliminated.

Conclusions: Once the giant cell tumor tissue was no longer exposed to denosumab, the stromal cells continued to proliferate in vitro, albeit to a lesser degree. However, they also showed almost complete loss of RANKL expression.

Clinical Relevance: It is clear that treatment with denosumab only partially addresses the therapeutic need of patients with a giant cell tumor by wiping out the osteoclasts but leaving the neoplastic stromal cells proliferative.

Case Reports in Medicine
Volume 2015, Article ID 767198, 6 pages
http://dx.doi.org/10.1155/2015/767198

Hindawi

Case Report

Two Cases of Sarcoma Arising in Giant Cell Tumor of Bone Treated with Denosumab

Cory Julian Broehm,[1] Erika L. Garbrecht,[2] Jeff Wood,[3] and Therese Bocklage[1]

[1]*Department of Pathology, University of New Mexico School of Medicine, MSC08 4640, 1 University of New Mexico, Albuquerque, NM 87131, USA*
[2]*Department of Orthopaedics, University of New Mexico School of Medicine, MSC10 5600, Albuquerque, NM 87131, USA*
[3]*Department of Radiology, University of New Mexico School of Medicine, MSC10 5530, 1 University of New Mexico, Albuquerque, NM 87131, USA*

Clin Orthop Relat Res (2015) 473:3050–3055
DOI 10.1007/s11999-015-4249-2

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

CrossMark

CASE REPORT

A High-grade Sarcoma Arising in a Patient With Recurrent Benign Giant Cell Tumor of the Proximal Tibia While Receiving Treatment With Denosumab

Luis A. Aponte-Tinao MD, Nicolas S. Piuzzi MD, Pablo Roitman MD, German L. Farfalli MD

GIANT CELL TUMOUR

DENOSUMAB

- REDUCES PAIN
- DECREASES VASCULARITY
- EASES RESECTION
- MAY INCREASE RISK OF LOCAL RECURRENCE AFTER CURETTAGE
- NO ROLE IN ADJUVANT SETTING
- LONG TERM THERAPY IN UNRESECTABLE CASES
- NO CONSENSUS ON DOSING SCHEDULE

Clin Orthop Relat Res (2018) 0:1-10
DOI 10.1007/s11999.0000000000000243

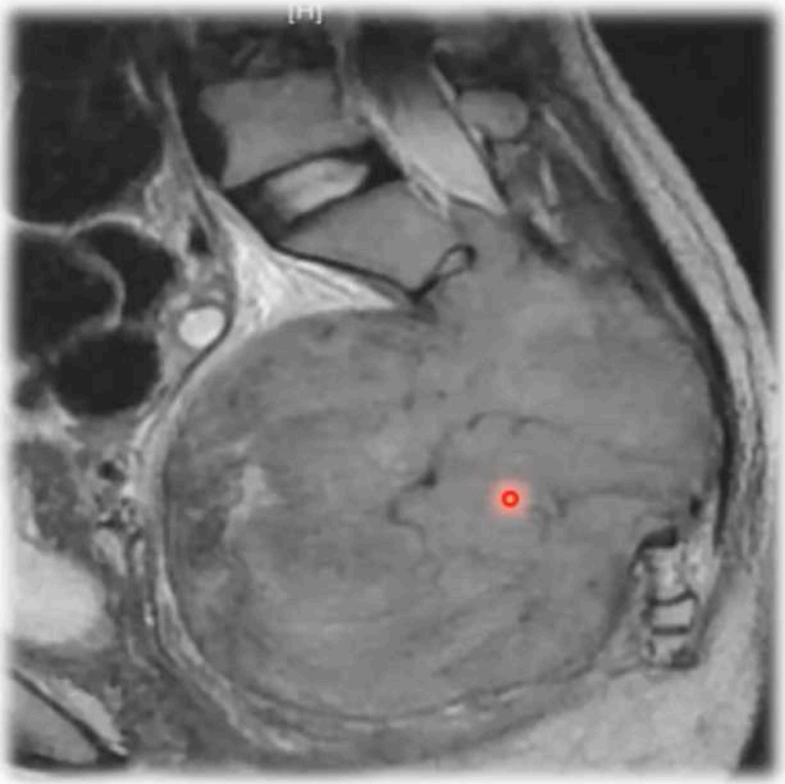
Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

2017 International Society of Limb Salvage Proceedings

Does Denosumab Change the Giant Cell Tumor Treatment Strategy? Lessons Learned From Early Experience

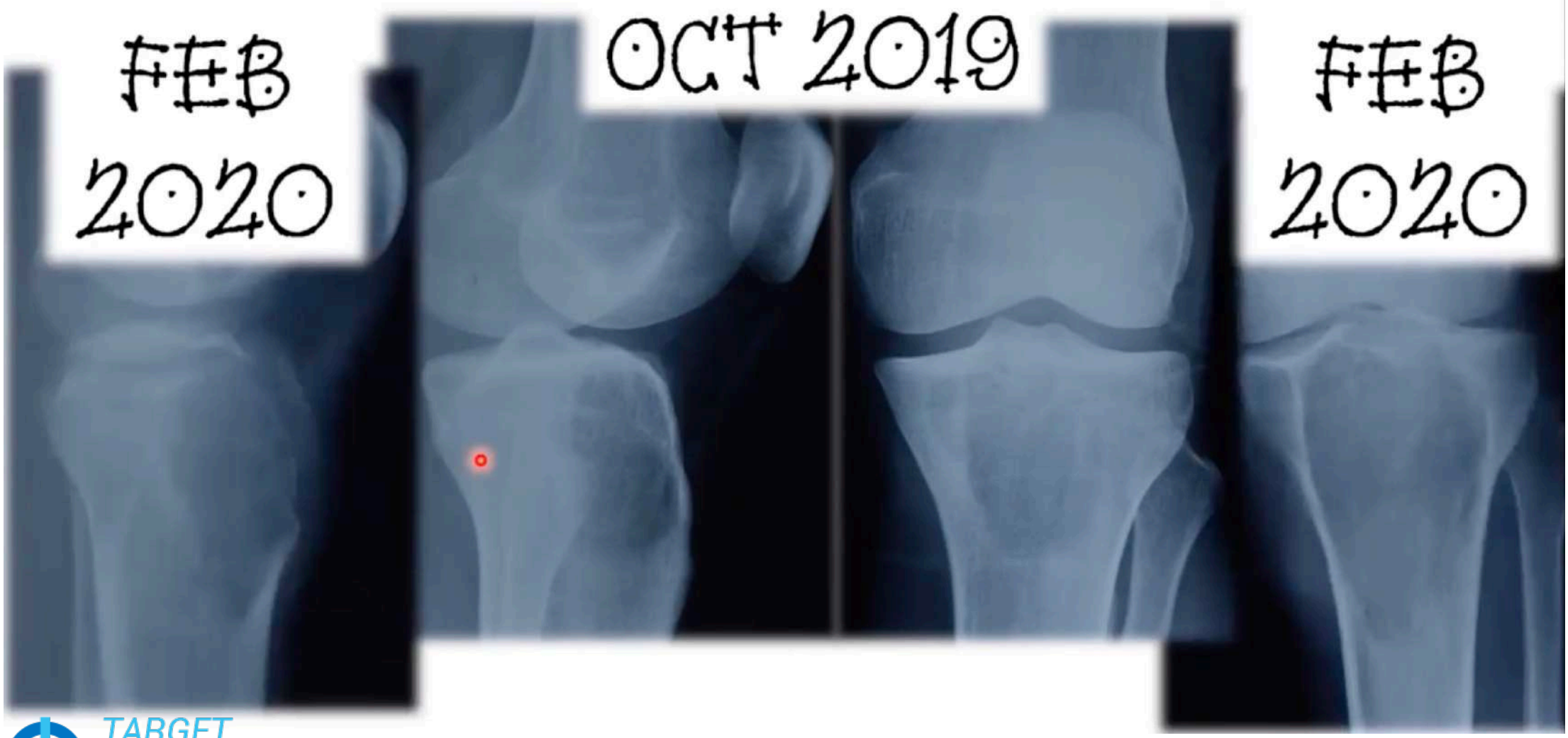
Manish G. Agarwal MS Orth, Manit K. Gundavda DNB Orth, Rajat Gupta MS Orth, Rajeev Reddy DNB Orth

UNRESECTABLE GCT

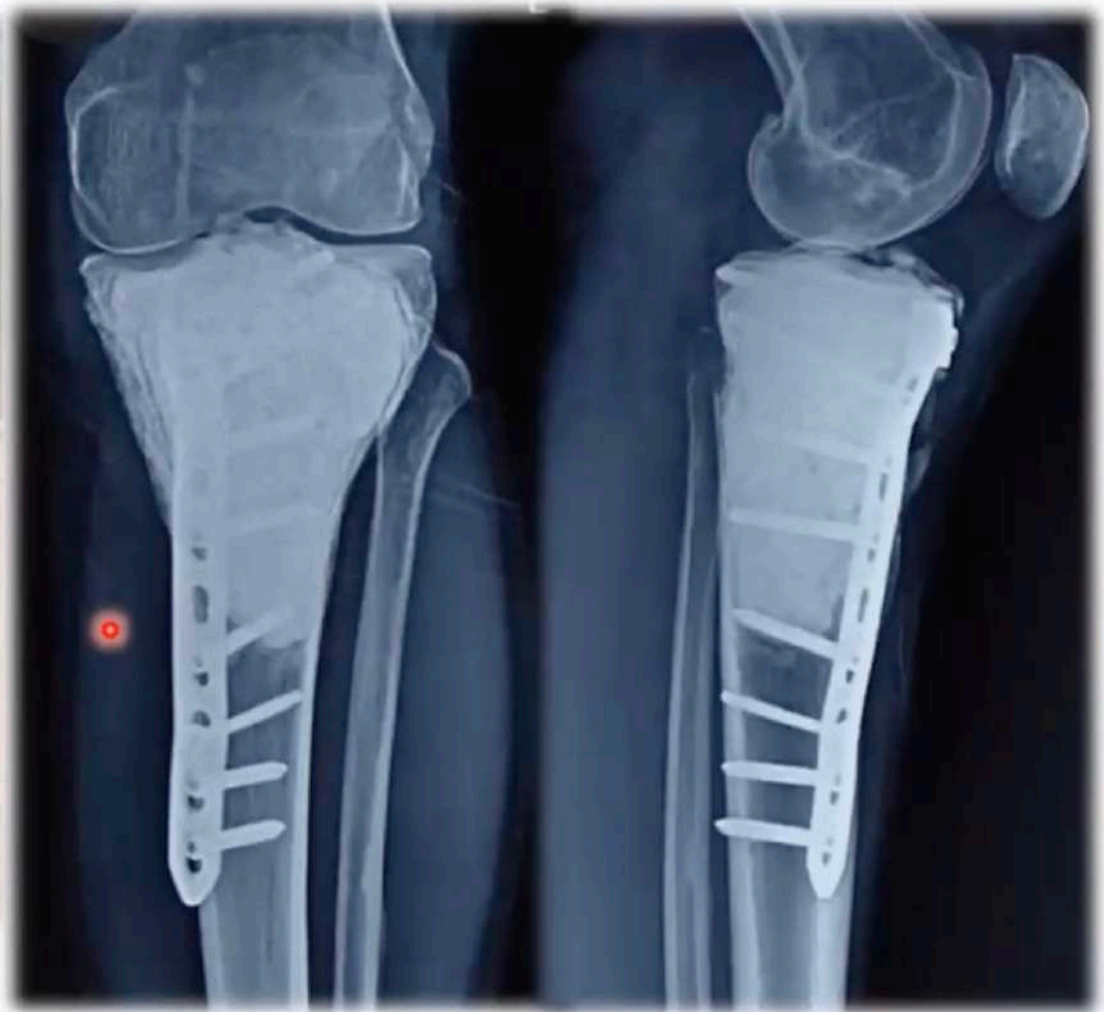


- ANGIOEMBOLISATION
- ZOLENDRONIC ACID
- DENOSUMAB
- RADIATION THERAPY

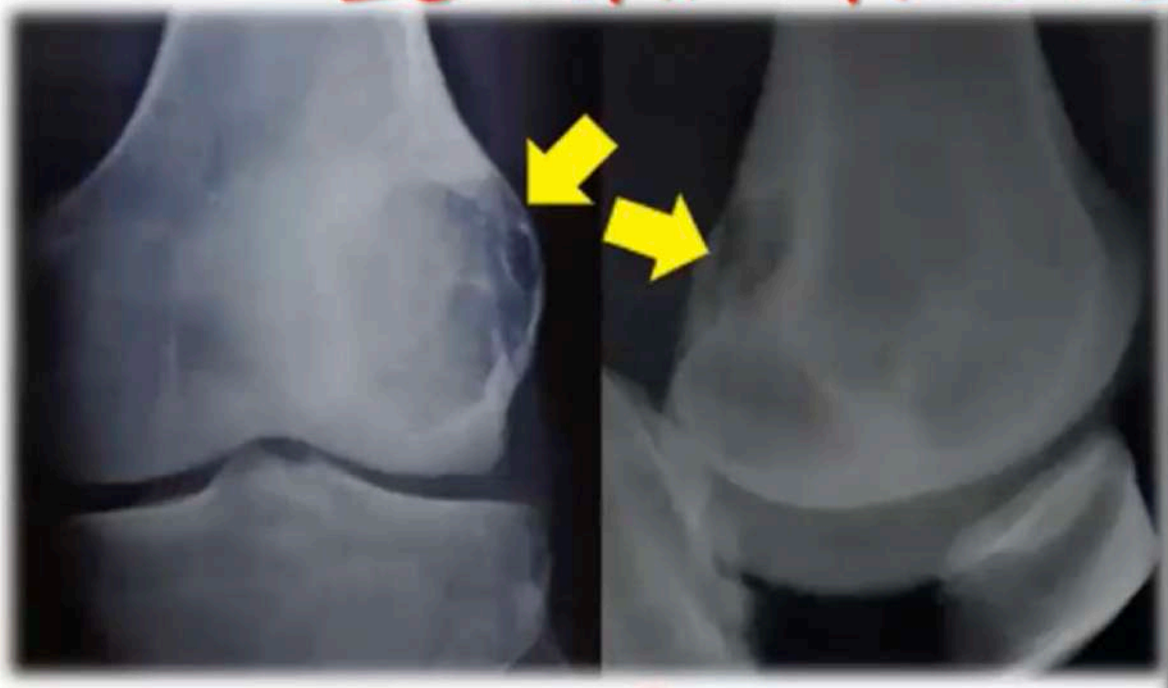
25 YEAR MALE WITH GCT KNEE

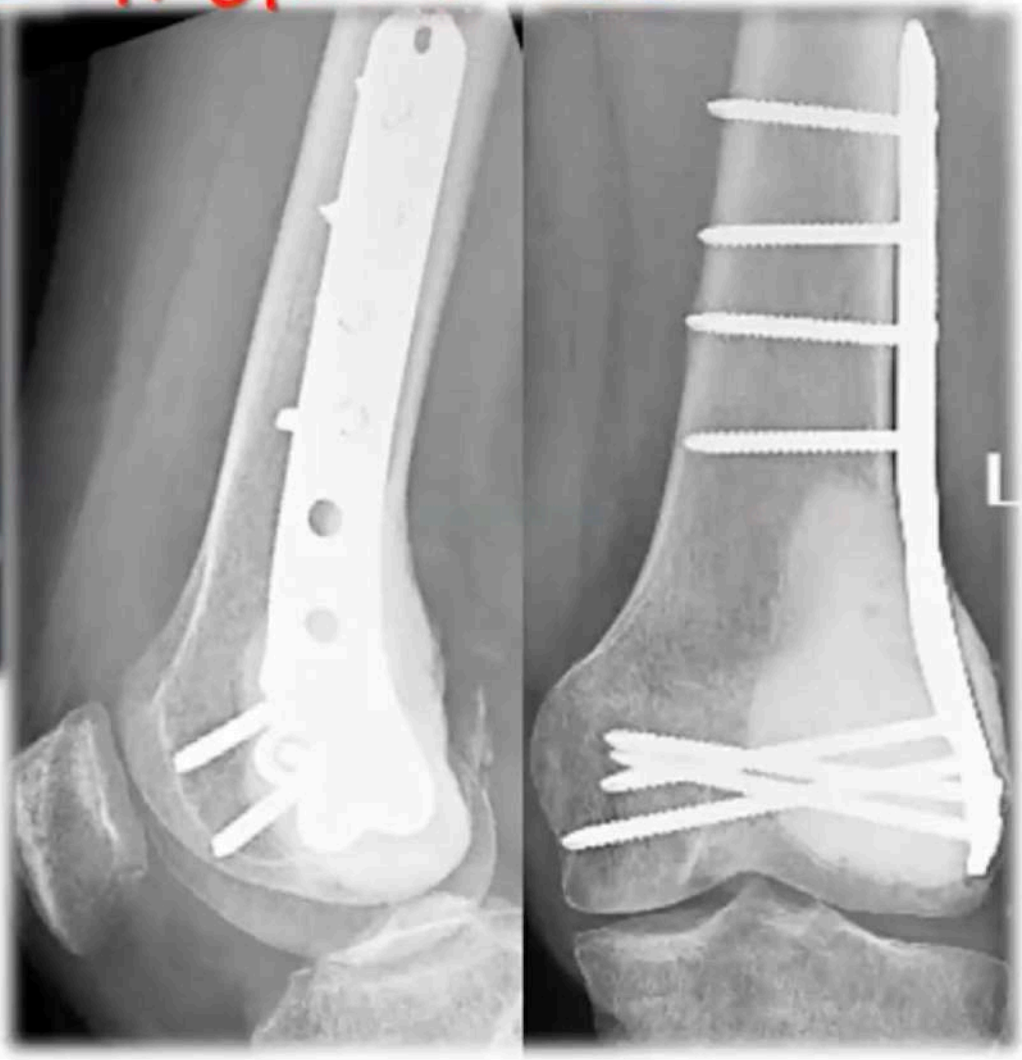


FUNCTION AT 18 MONTHS



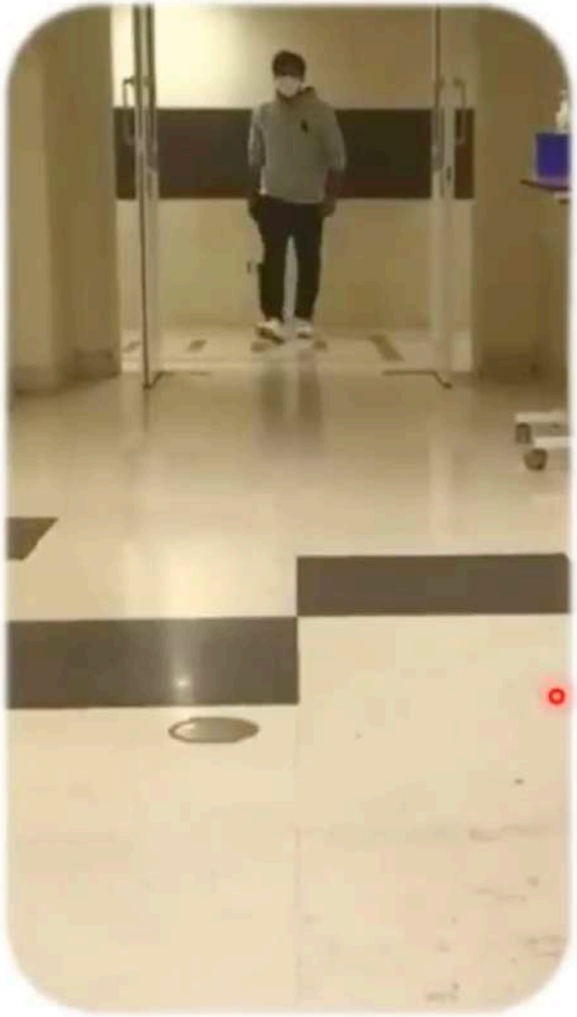
28 YEAR MALE WITH GCT KNEE

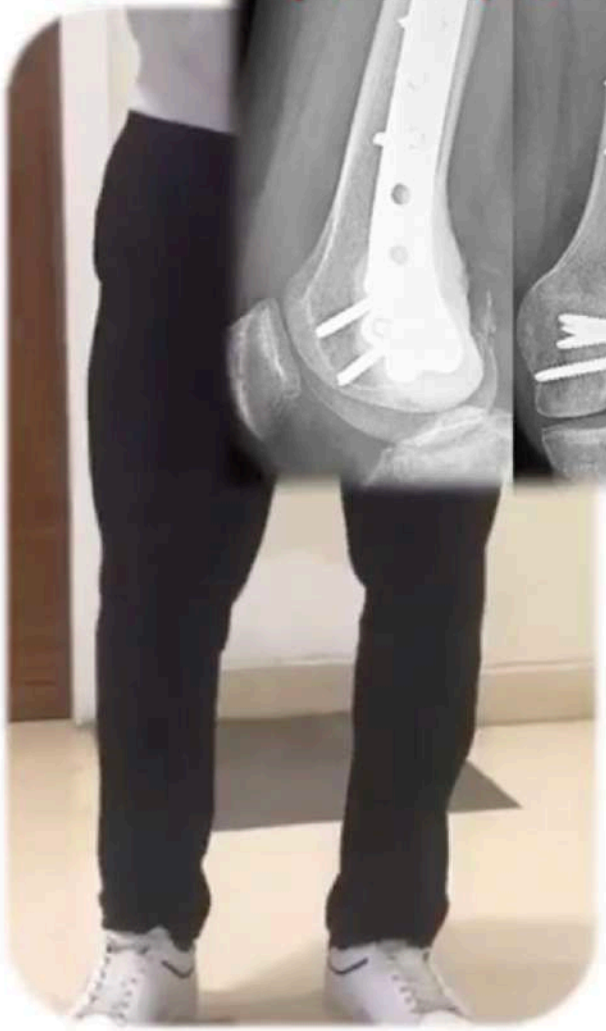


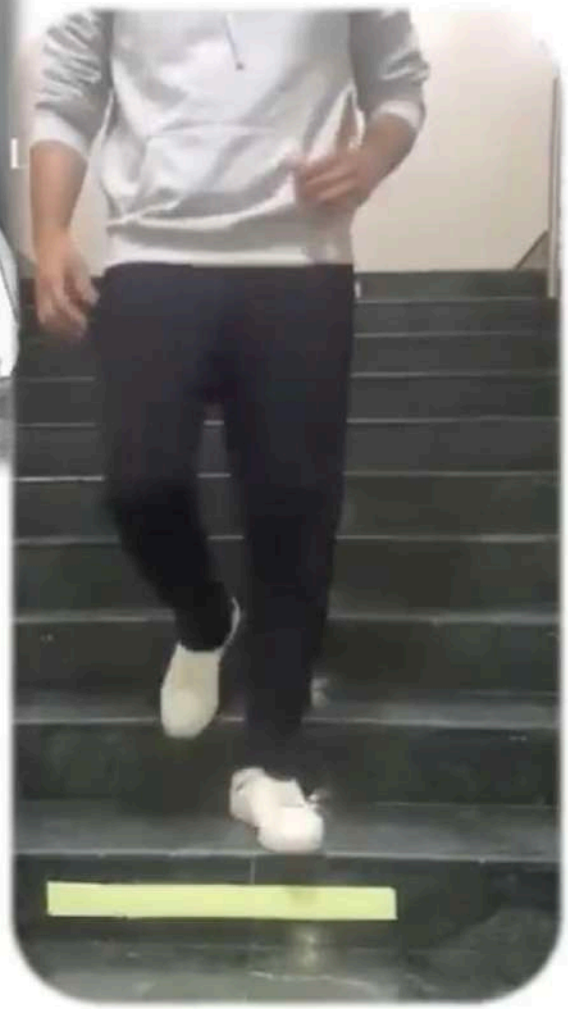


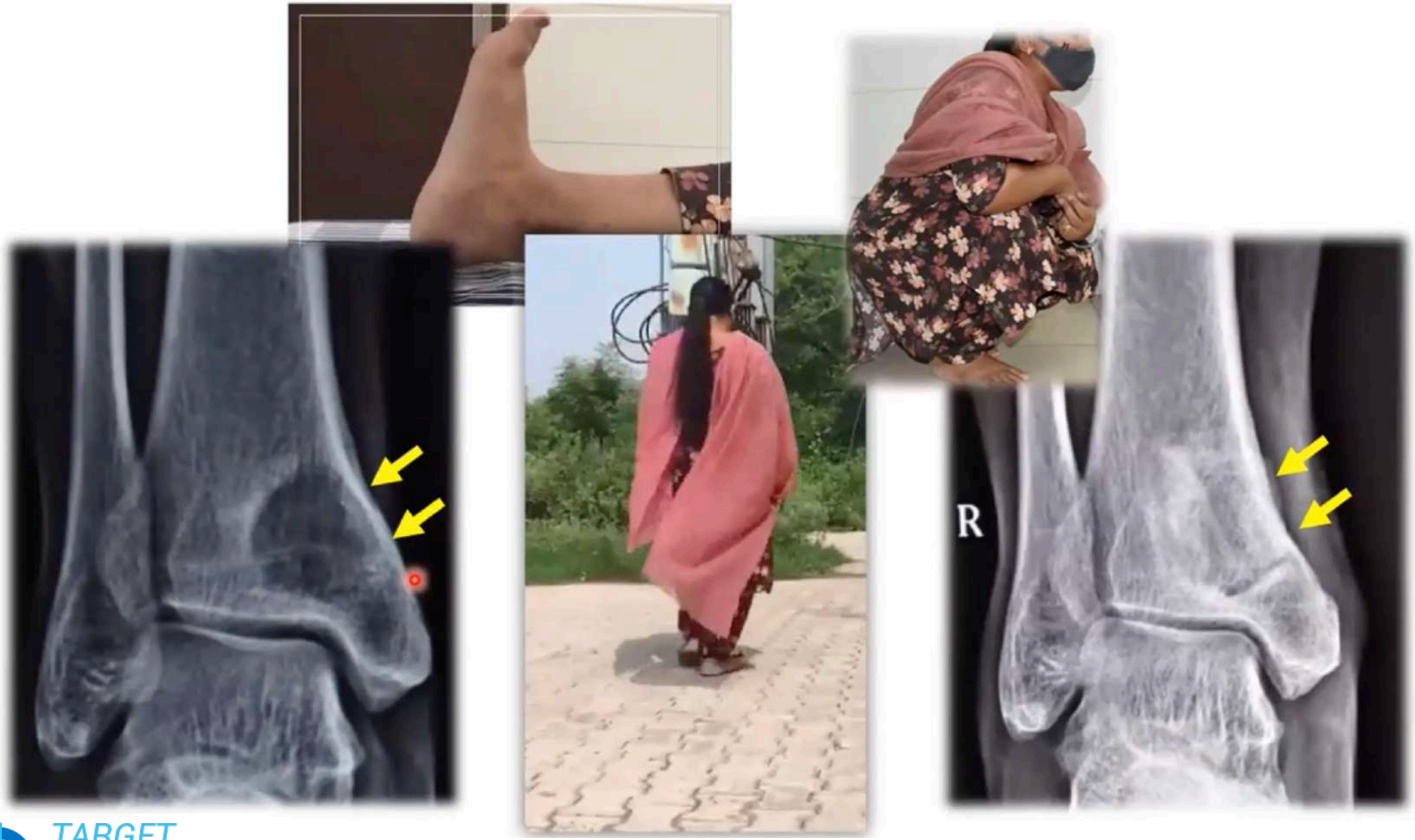
EXTENDED CURETTAGE & CEMENTING

FUNCTION AT 1.5 YEARS

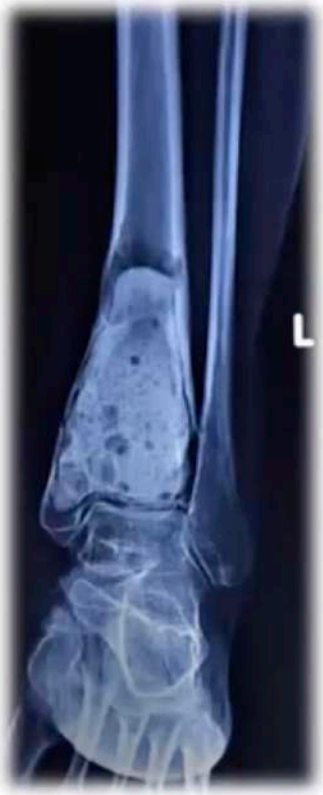


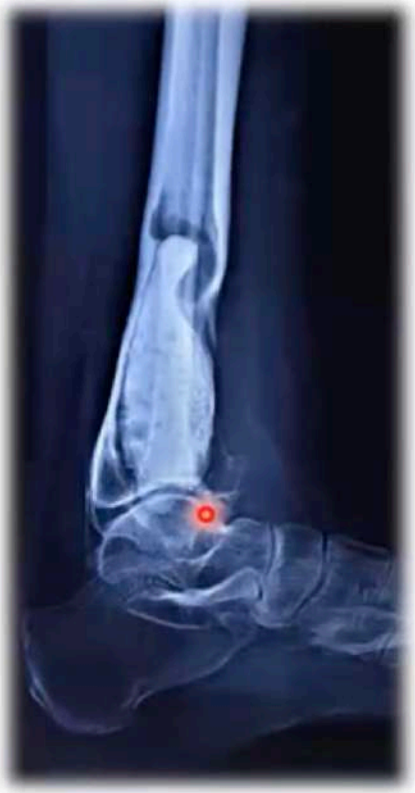


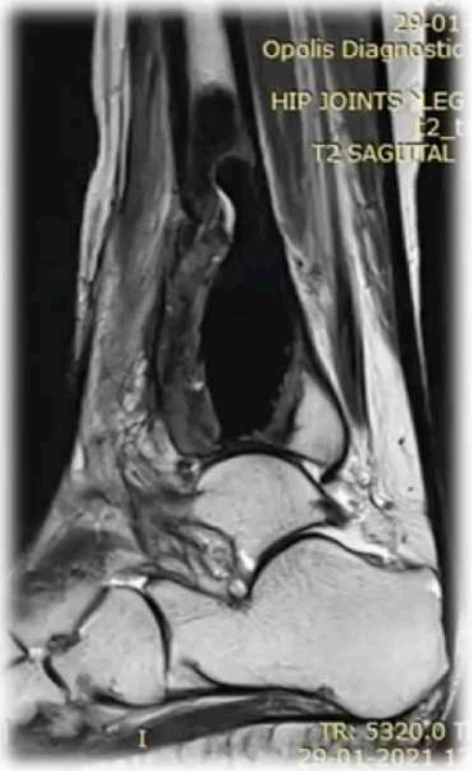


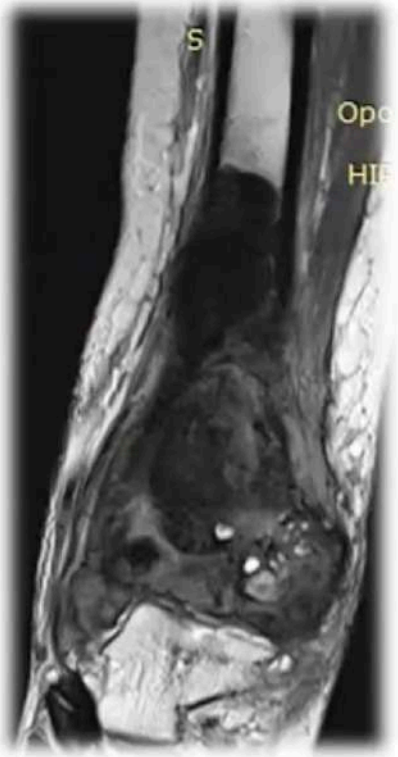


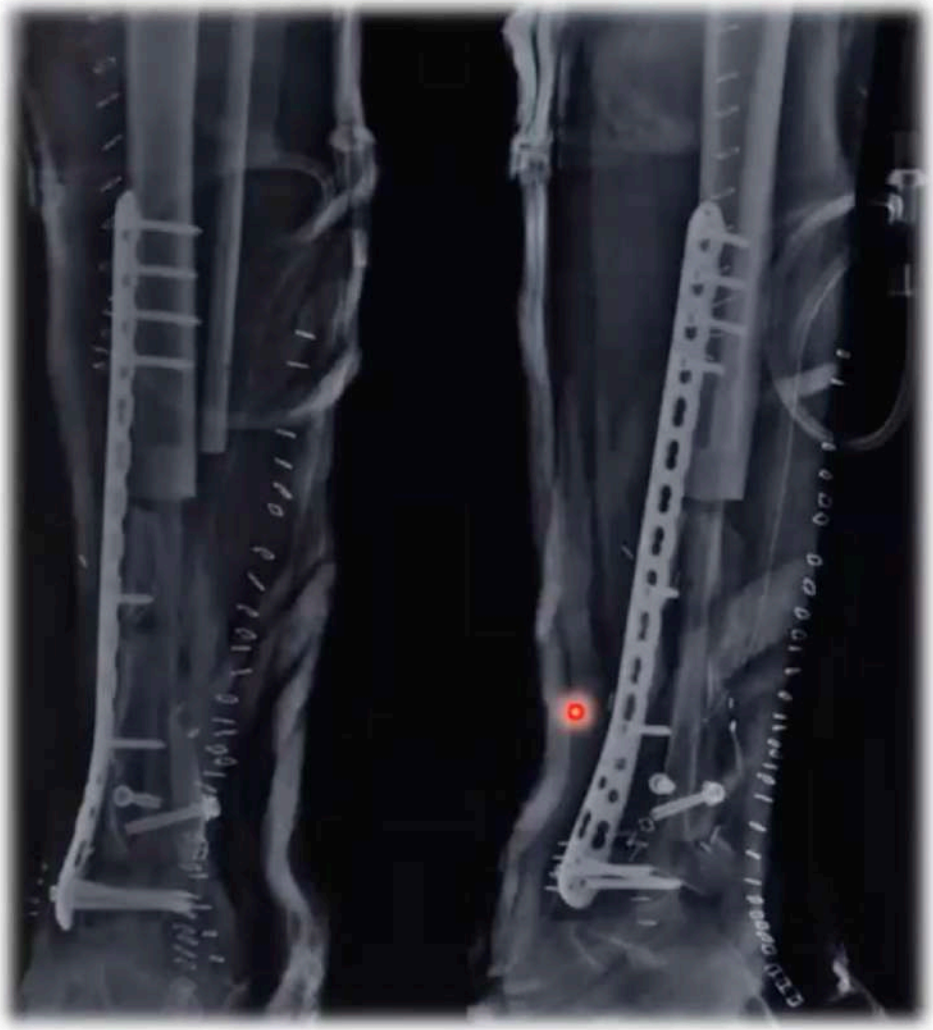
30y/F RECURRENT GCT DISTAL TIBIA











DISTAL TIBIA RESECTION

+

FROZEN AUTOGRAFT STERLISATION

+

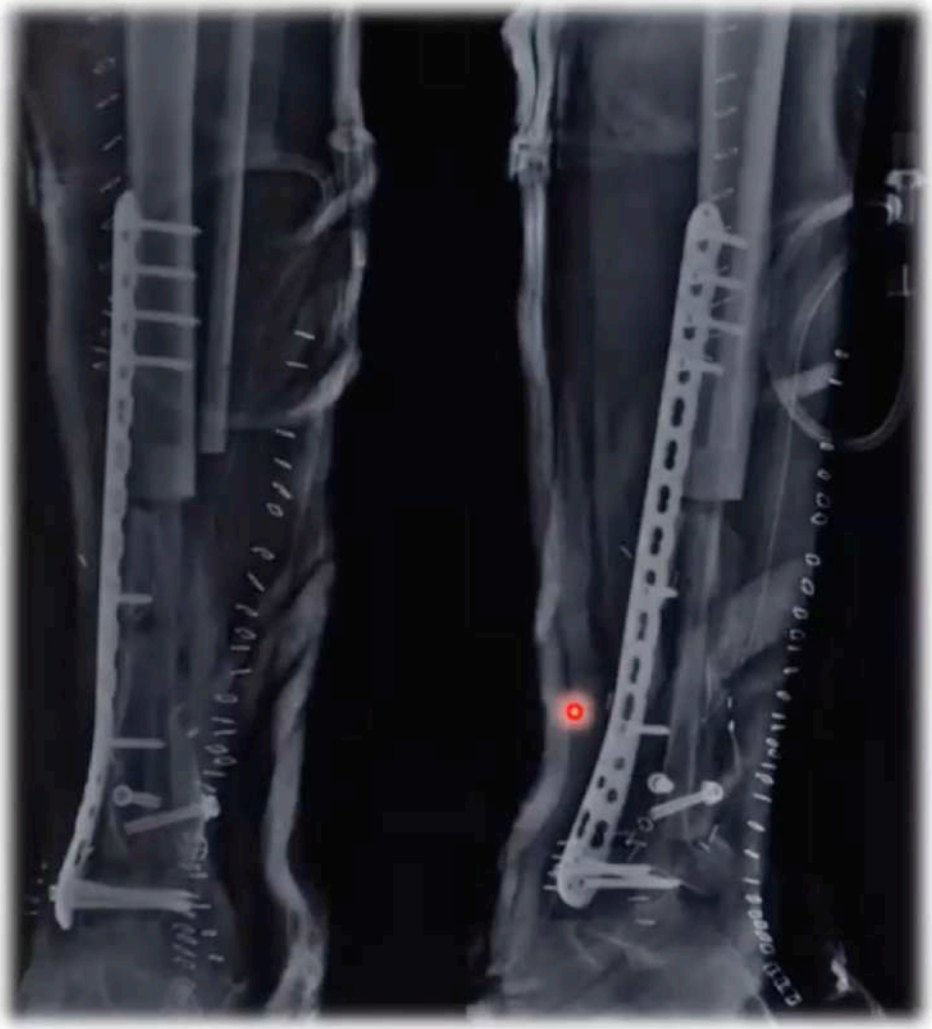
TIBIALISATION OF FIBULA

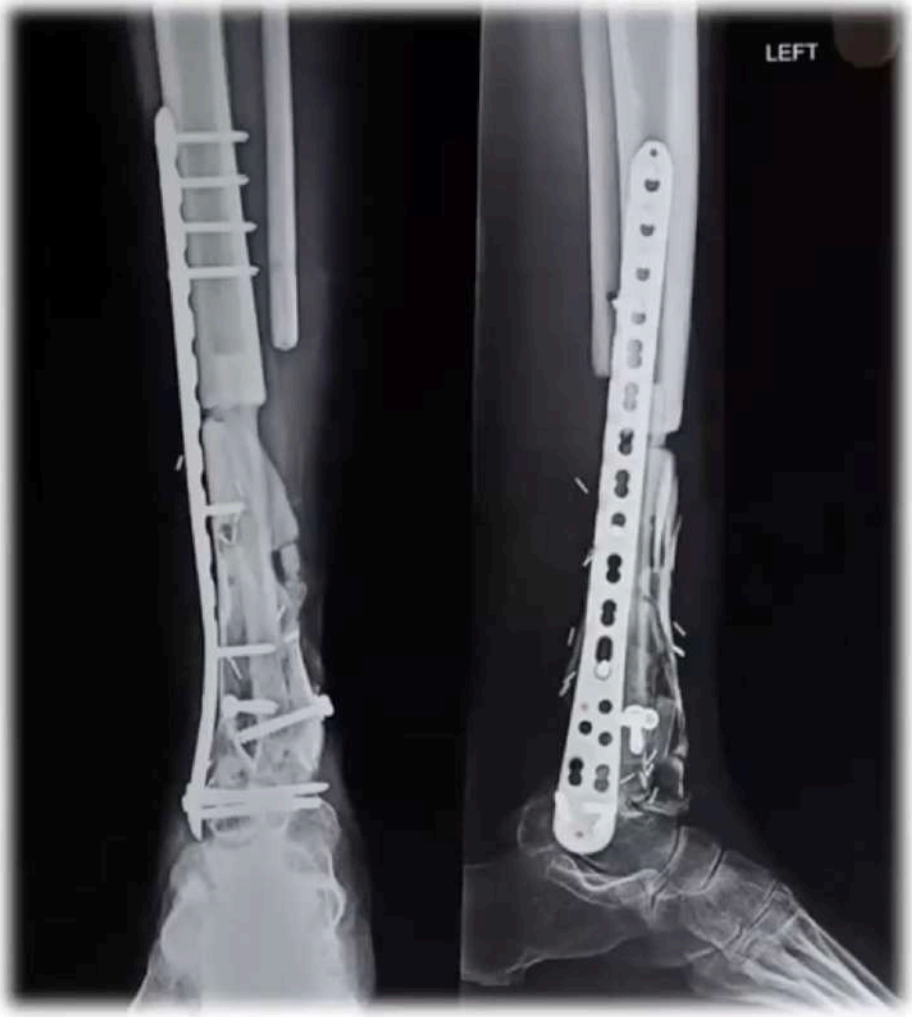
+

ILIAC CREST BONE GRAFTING

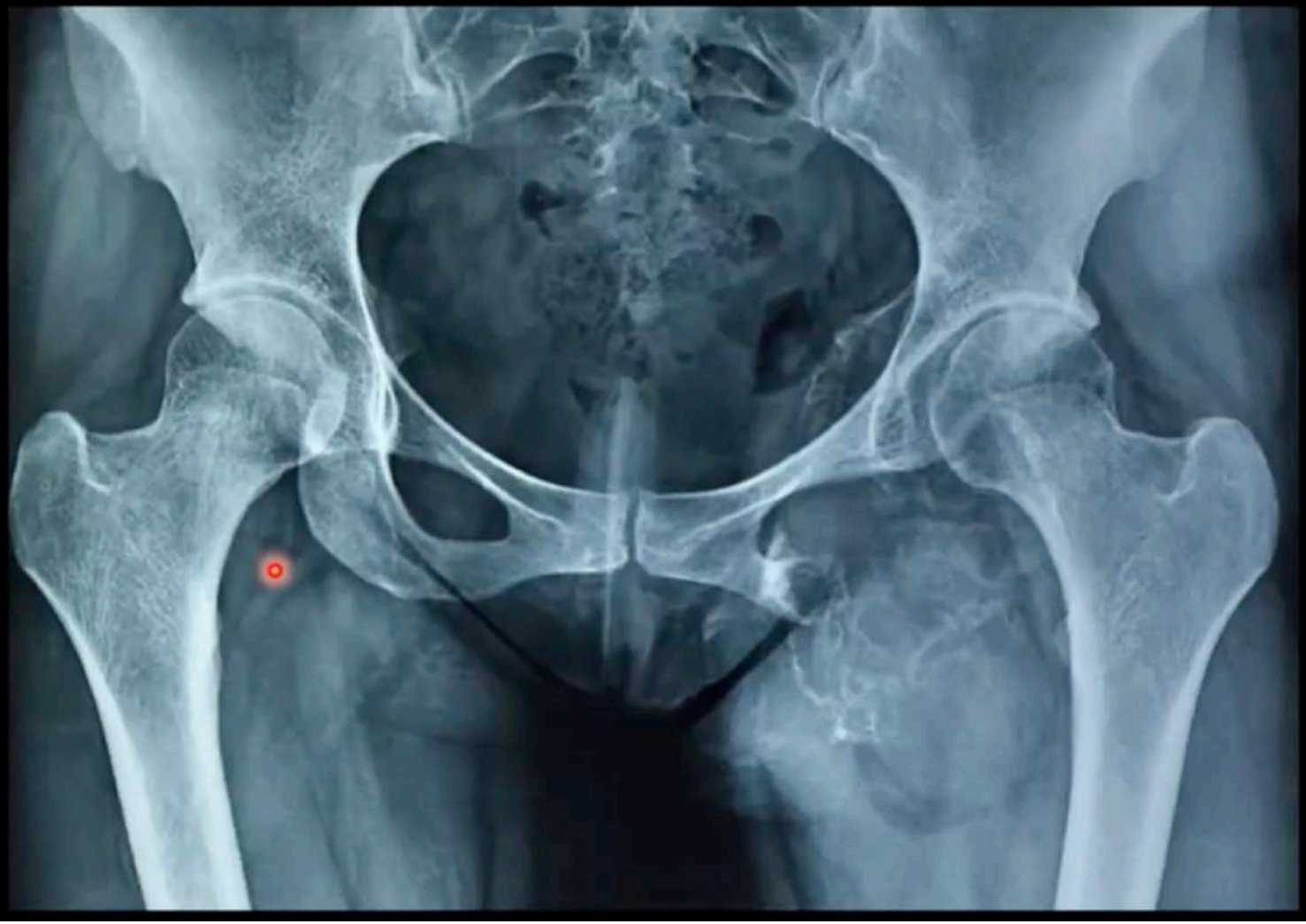
+

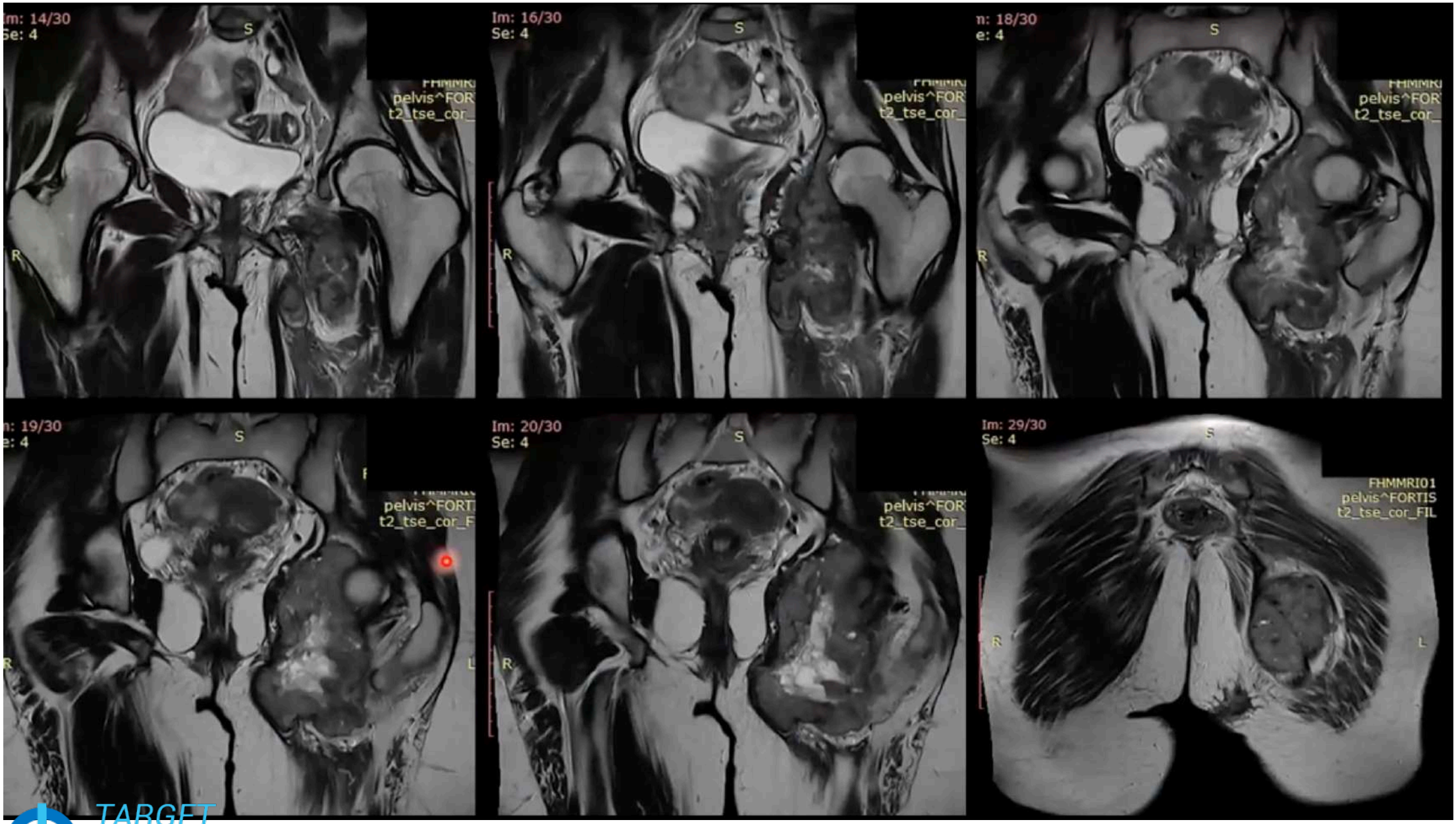
PLATING

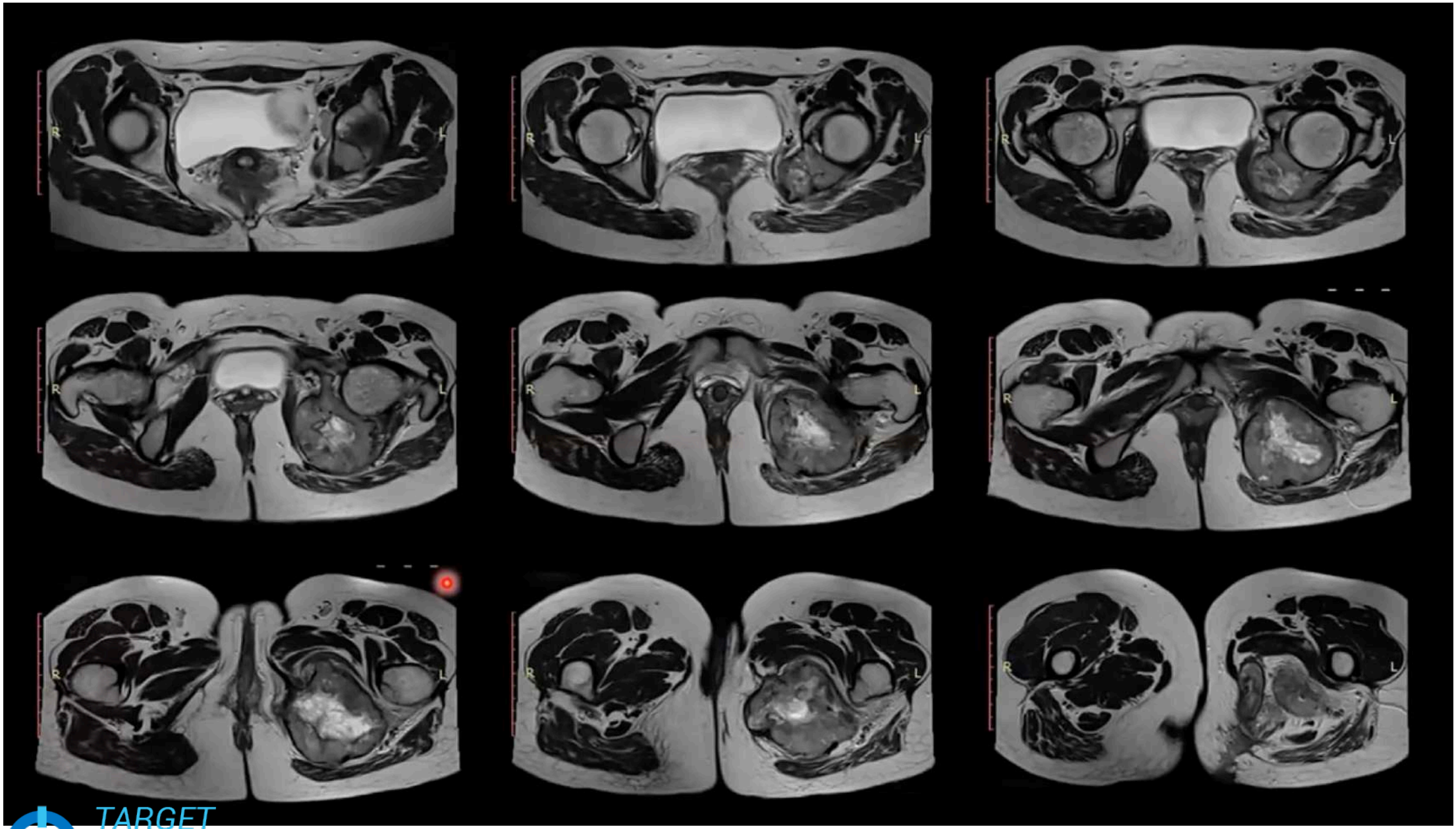


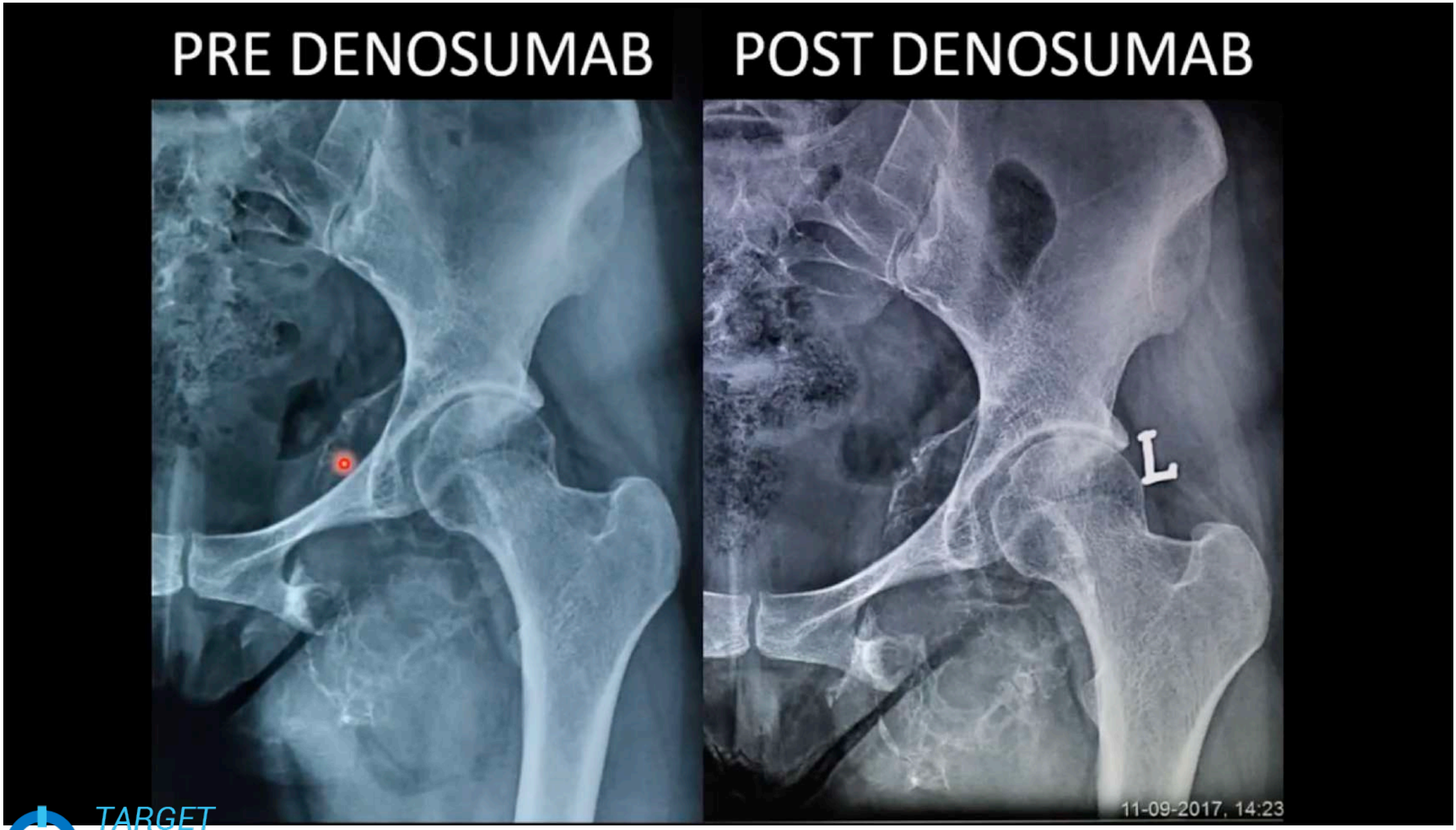


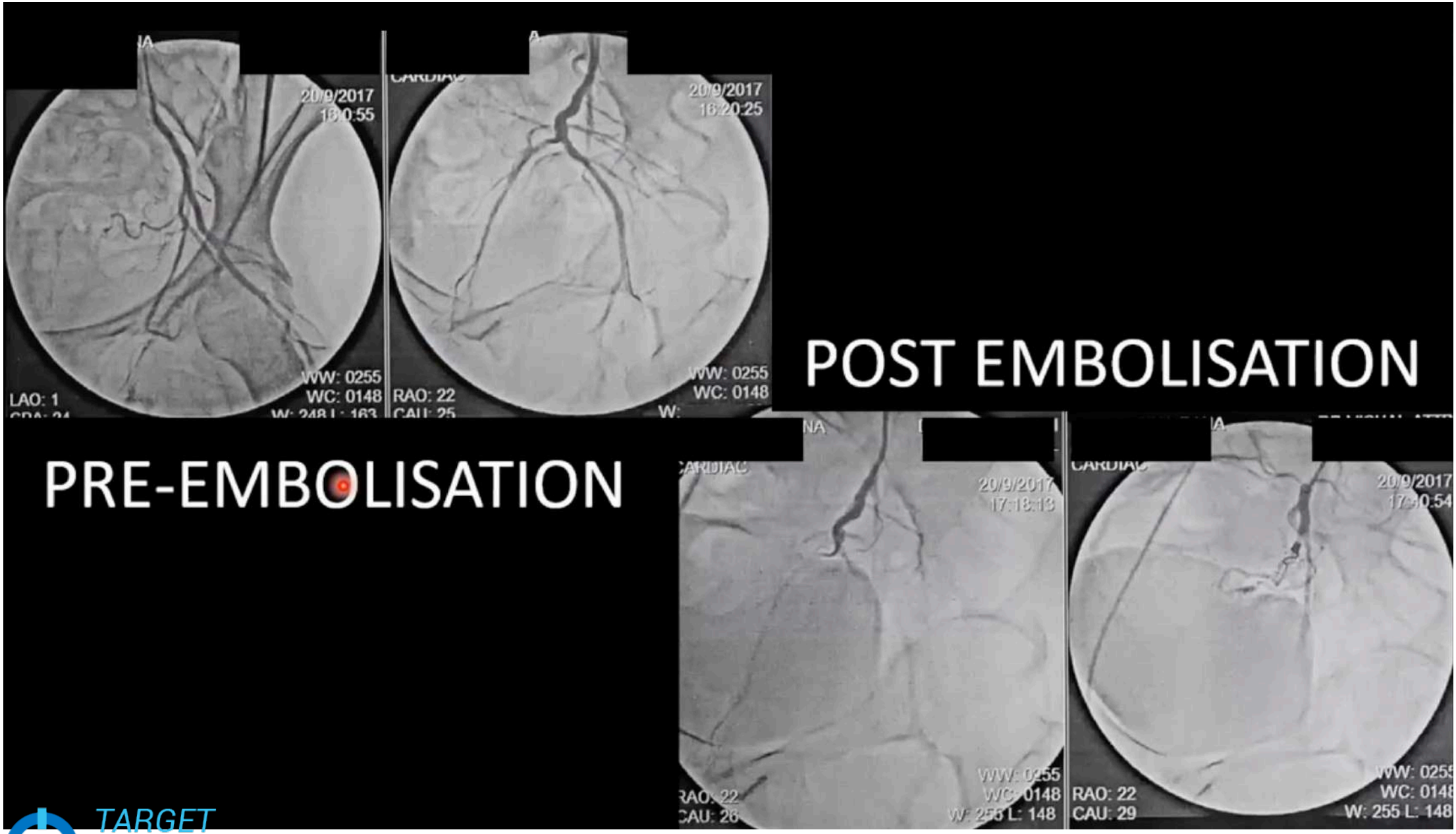
25Y /F RECURRENT GCT PELVIS



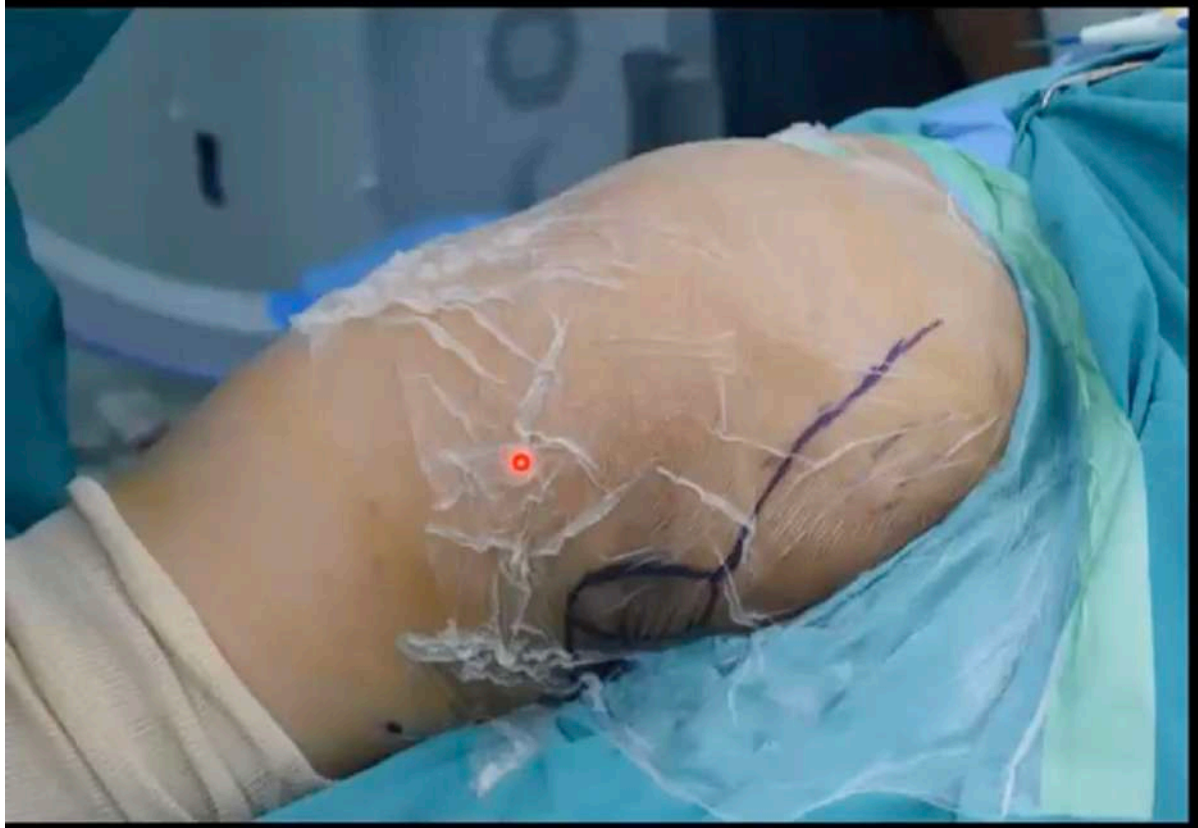


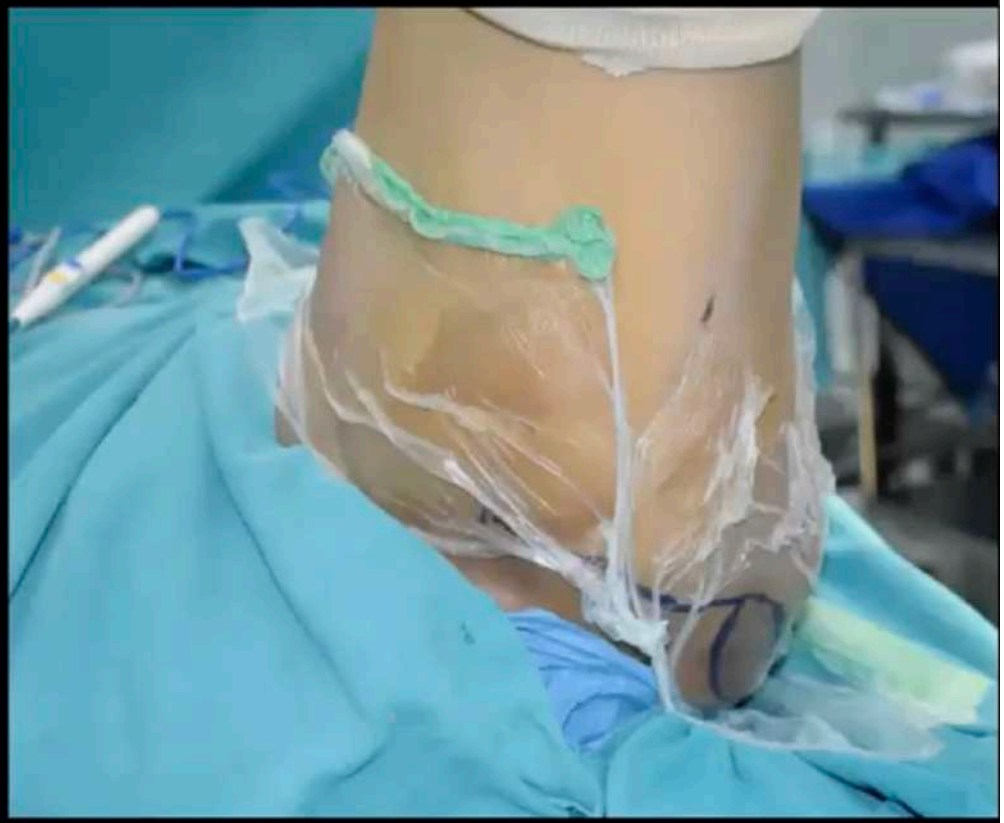


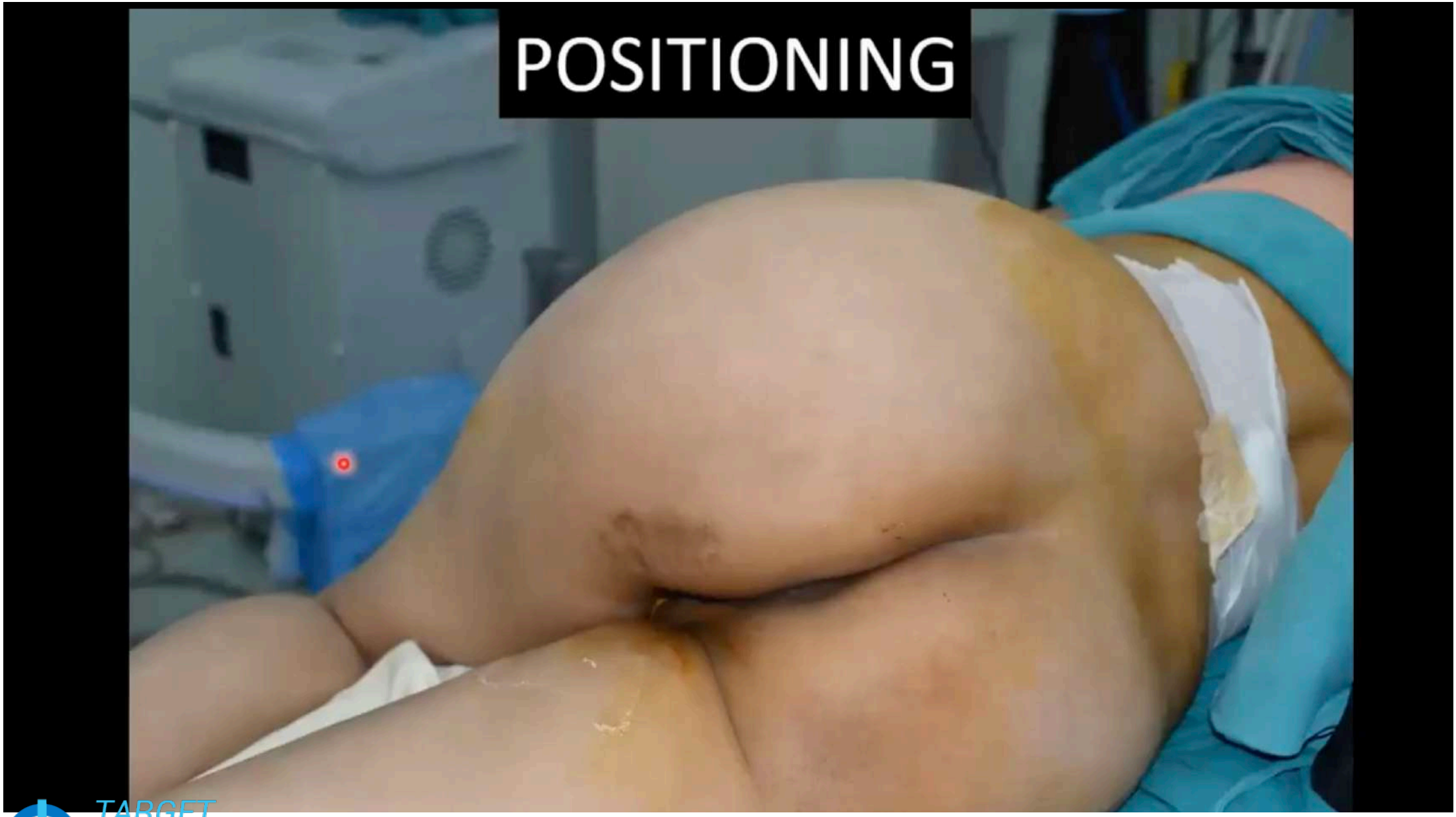


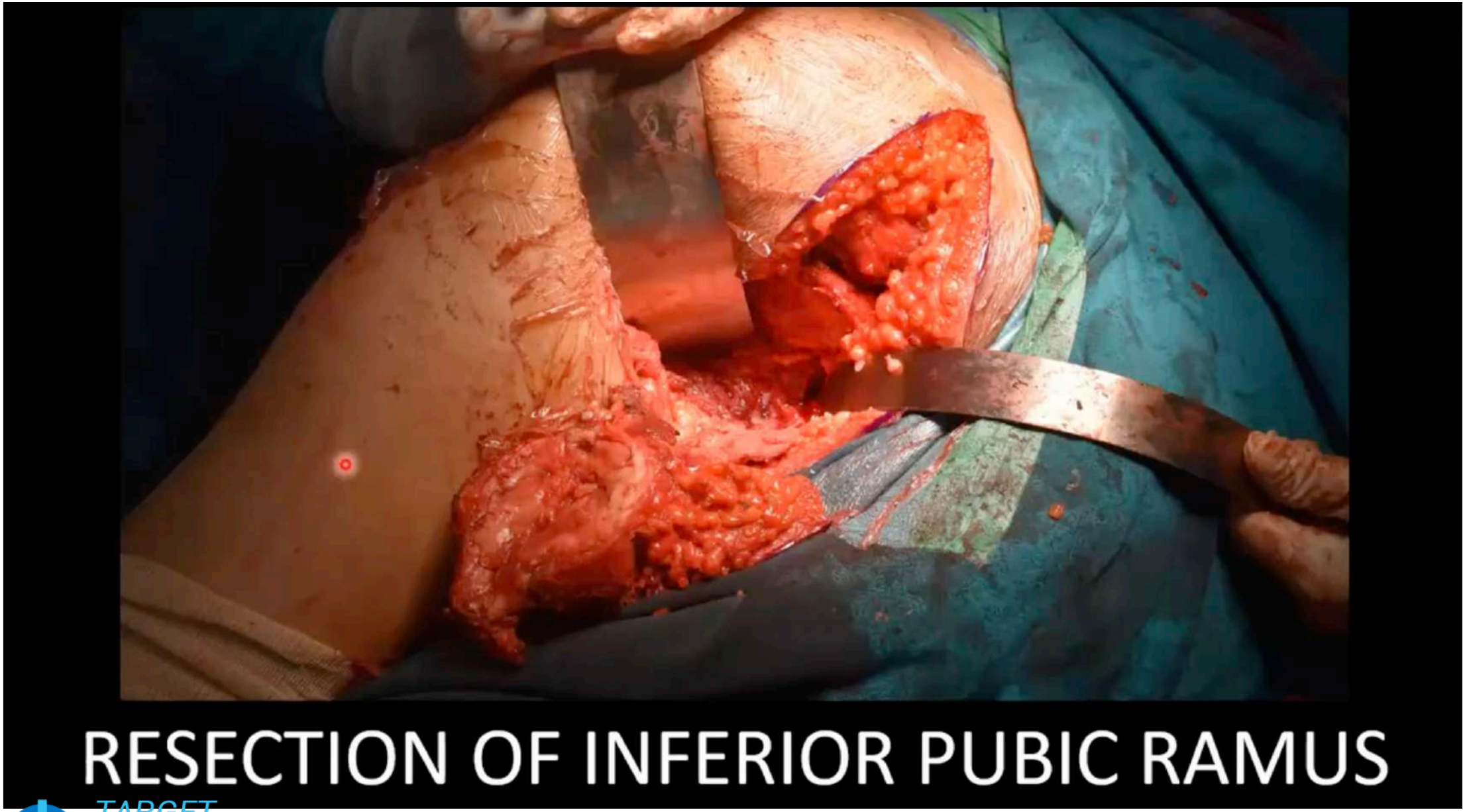


INCISION









EXTENDED CURETTAGE OF POSTERIOR ACETABULUM & SUPRA-ACETABULAR REGION