



### Introduction

Osteosarcoma (OSA) is the most common primary bone tumor in the dog. Current surgical limb-sparing options are limited to the distal radius and can have complications including implant failure, local tumor recurrence and infection. Stereotactic radiosurgery (SRS) is a novel and evolving treatment option that can be combined with adjuvant chemotherapy for patients with extremity OSA.[1] SRS delivers high dose curative-intent radiation to the tumor with a sharp decrease in dose to adjacent normal tissues. The Varian Trilogy™ linear accelerator at Colorado State University Veterinary Medical Center delivers image guided 3D conformal radiation with a high degree of precision.

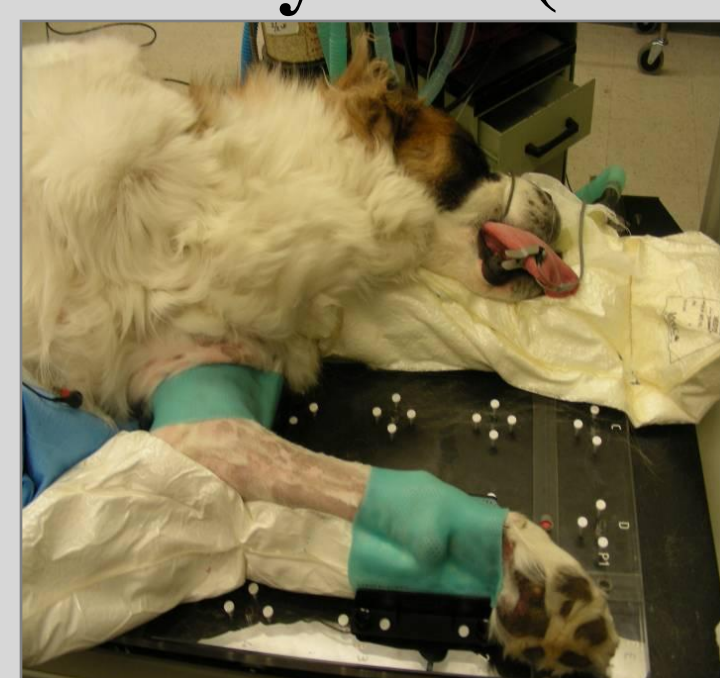
### Treatment Planning

❖ 2 systems of patient positioning and fixation were developed and used for radiation planning and treatment:

- Frame-based bone anchored system (n = 16)
- Non-invasive immobilization system (n = 9)

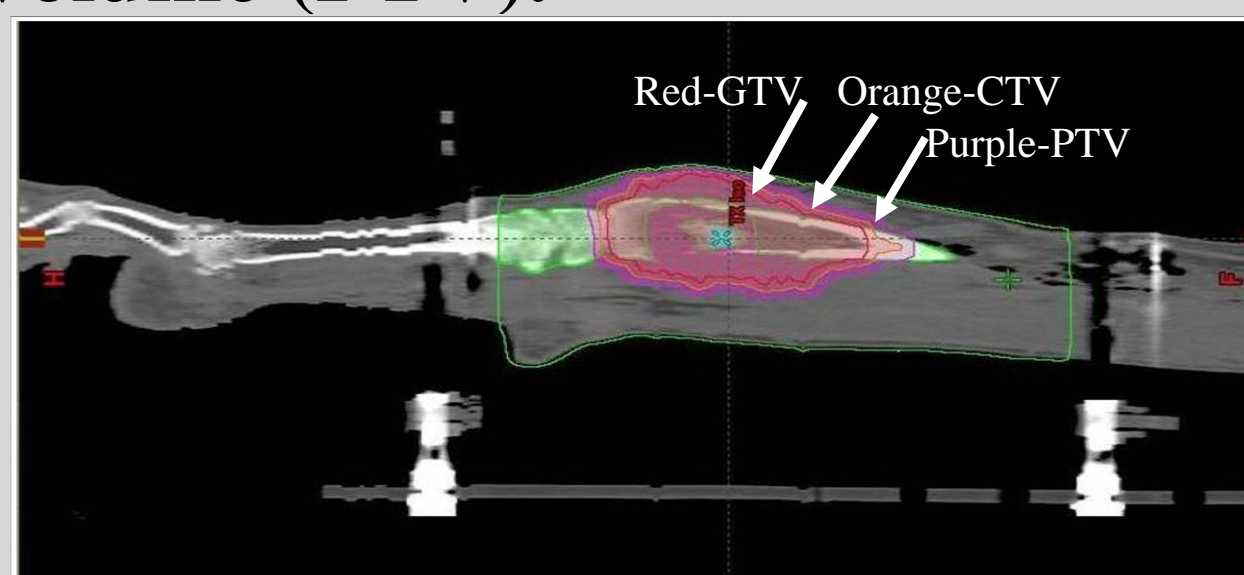


Frame-based system

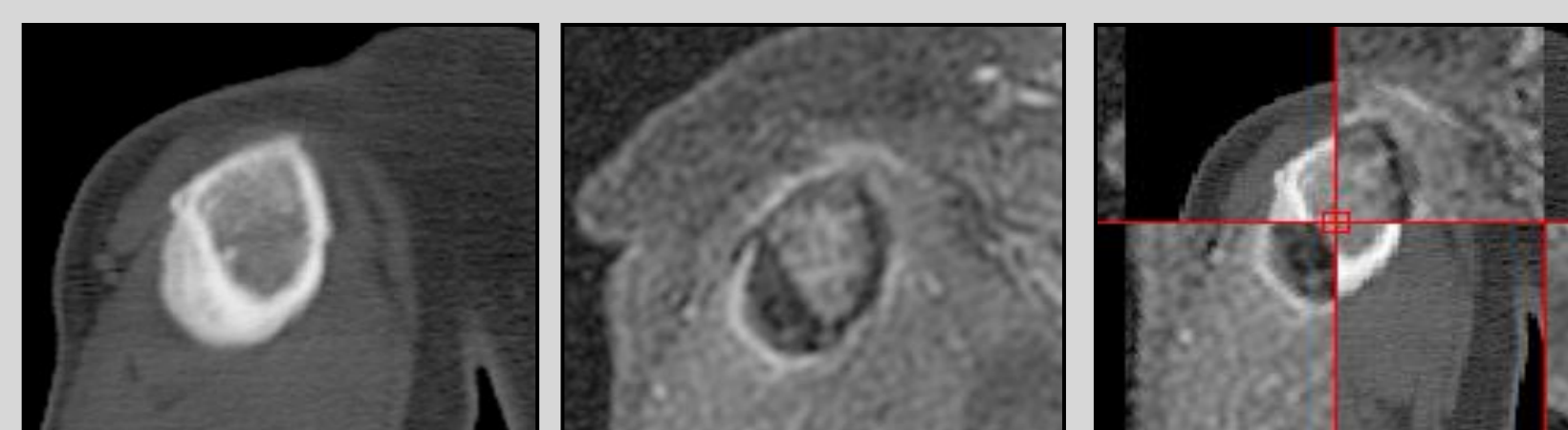


Non-invasive system

❖ The Varian Eclipse Treatment planning system was used to develop the radiation treatment plans. The lesion and bone outline are identified and the Gross Tumor Volume (GTV) defined. Expansions of 2 mm are then made for the Clinical Tumor Volume (CTV) and Planned Tumor Volume (PTV).



❖ We used image fusion of pretreatment MRI and CT images in 1 case. This allows better delineation of the soft tissue and bone marrow components of the tumor, providing optimal treatment planning.



Transverse CT, MRI and fused registered images

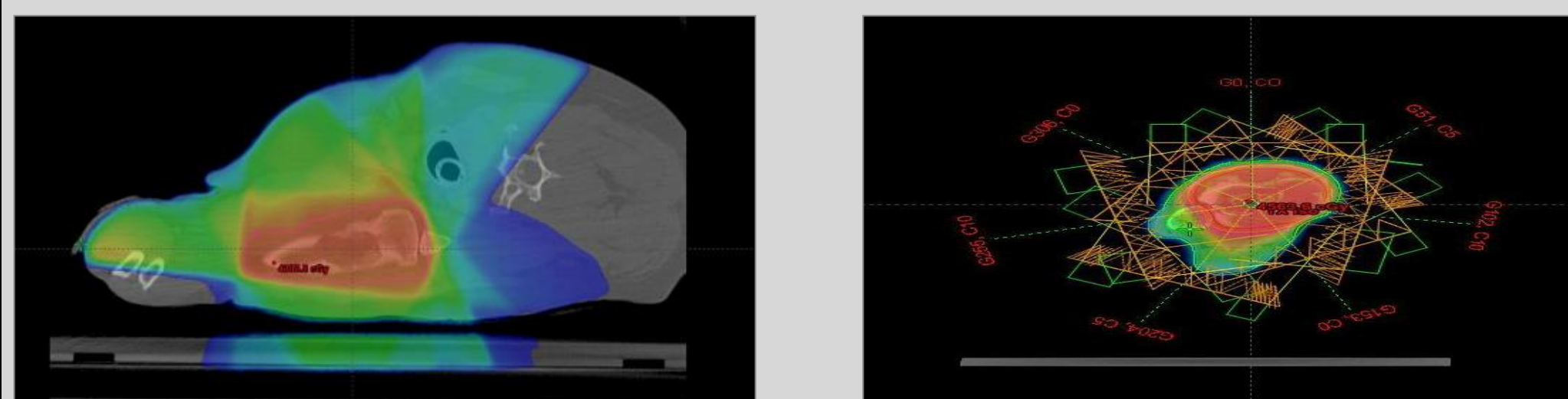
### Treatment Protocol

❖ At each treatment session, the patient was anesthetized, positioned and secured in the exact manner as for the planning CT.

❖ Orthogonal view kVp images were obtained from the Trilogy onboard imaging system and 2D/2D matching of bony landmarks to the planning CT performed.

❖ Radiation was delivered using a hypofractionated protocol:

- 2-3 fractions, 1-3 days between fractions
- 5-7 static fields of radiation were used
- Total dose to tumor volume = 32-42 Gy



Color wash maps showing the sharp decrease in dose  
The right image shows the 7 radiation fields used.

❖ The skin dose was modified to no more than 0.5% of the skin receiving more than 35 Gy after identifying a Grade 3 skin effect in our first patient.

❖ Pamidronate (1 mg/kg IV) was delivered before and after SRS to reduce incidence of pathologic fracture.

❖ Carboplatin (300 mg/m<sup>2</sup> IV) was delivered 1 hour before the 1<sup>st</sup> or 2<sup>nd</sup> SRS fraction for potential radiosensitizer effect

❖ Adjuvant chemotherapy continued after SRS:

- Single-agent carboplatin or
- Carboplatin / Doxorubicin combination

❖ Monthly follow-up radiographs of lesion site + thoracic radiographs every 3 months to monitor for metastasis

❖ Response to therapy was assessed by:

- Clinical function
- Radiographs
- Bone-turnover biomarkers: urine serum NTx
- % tumor necrosis of retrieved specimens

### Patient Signalment + Lesion Distribution

❖ 25 client-owned dogs received SRS treatment of their 1<sup>st</sup> or metastatic OSA of the appendicular limb:

- Mean age = 8.6 years
- Median follow-up time = 133 days
- Number of patients alive = 20
- Distal radius (n = 9), ulna (n = 2)
- Proximal humerus (n = 10)
- Distal tibia (n = 2)
- Distal femur (n = 2)

### Results

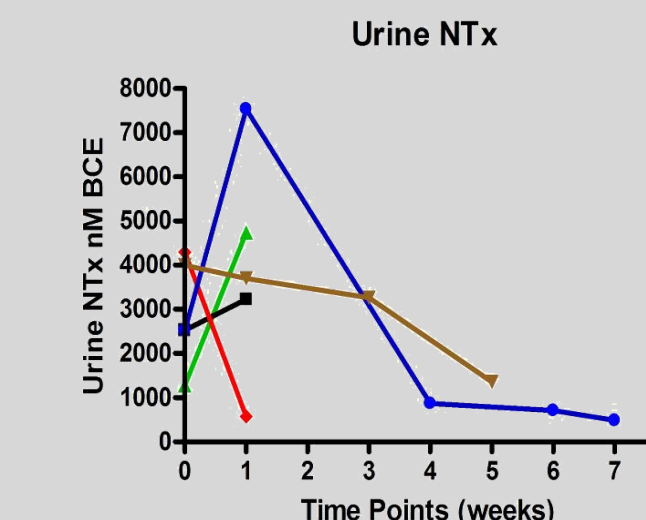
❖ The positioning systems provided highly repeatable and accurate patient positioning.

❖ We have successfully treated tumors in anatomic sites that were previously not amenable to surgical limb salvage procedures.

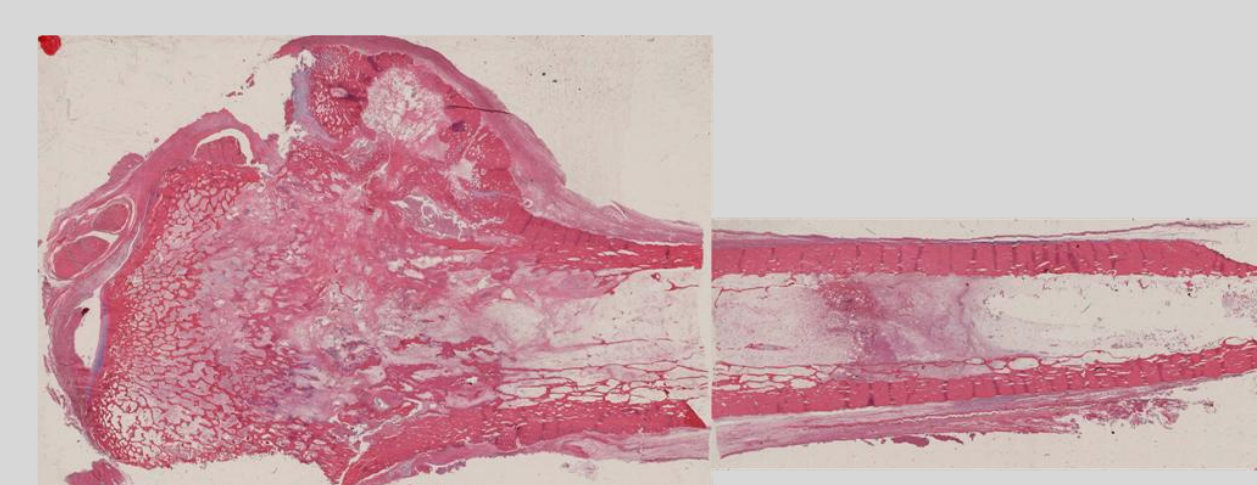
❖ Clinical outcome has been good to excellent based on the following parameters:

- Durable pain palliation in all patients
- Decreased lameness as observed by owners and clinicians in all patients
- No evidence of local tumor recurrence on follow-up radiographs in all patients
- Decreasing trend in bone turnover biomarkers

- Urine NTx levels returned to normal by 4 weeks post SRS



- Effective percent tumor necrosis (n = 5)



Histology of Lesion showing 100% tumor necrosis

- Evidence of local tumor control documented by nuclear scintigraphy (n = 2)



October 2008:  
Pre-SRS scans

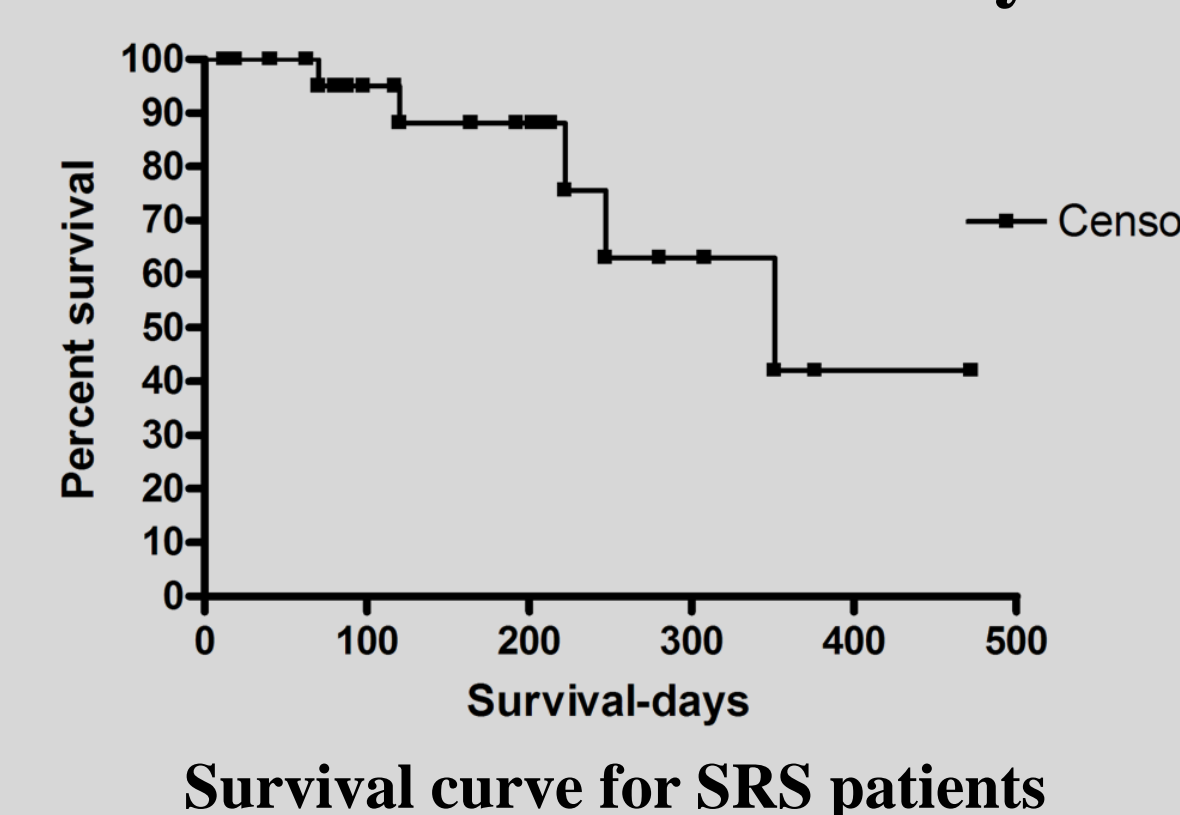
April 2009:  
Photopenic bone in treatment fields

- Metastasis--5 patients developed definitive metastatic disease:

- Pulmonary metastasis (n = 2)
- Bony metastasis (n = 2)
- Both pulmonary + bony metastasis (n = 1)

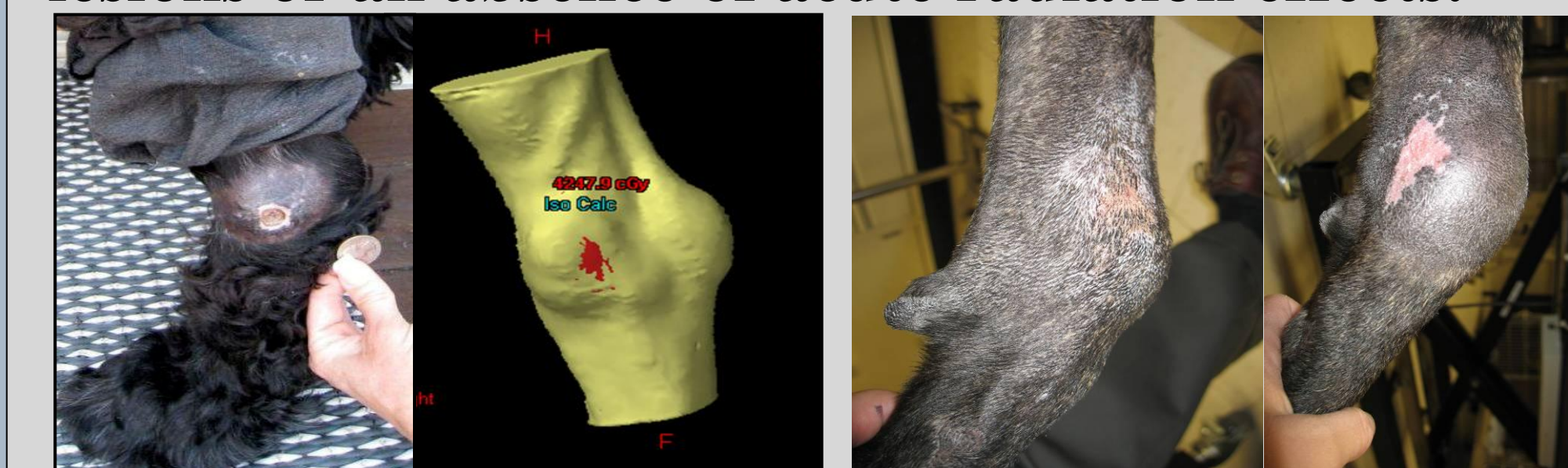
- Disease-free interval = 121 days

- Median survival time = 351 days



### Complications

❖ Focal acute and late skin radiation effects occurred in 5 cases. After the Grade 3 skin effect seen in the 1st patient, the radiation dose to the skin was decreased to a maximum of 35 Gy, which reduced the skin effects to mild focal Grade 1 lesions or an absence of acute radiation effects.



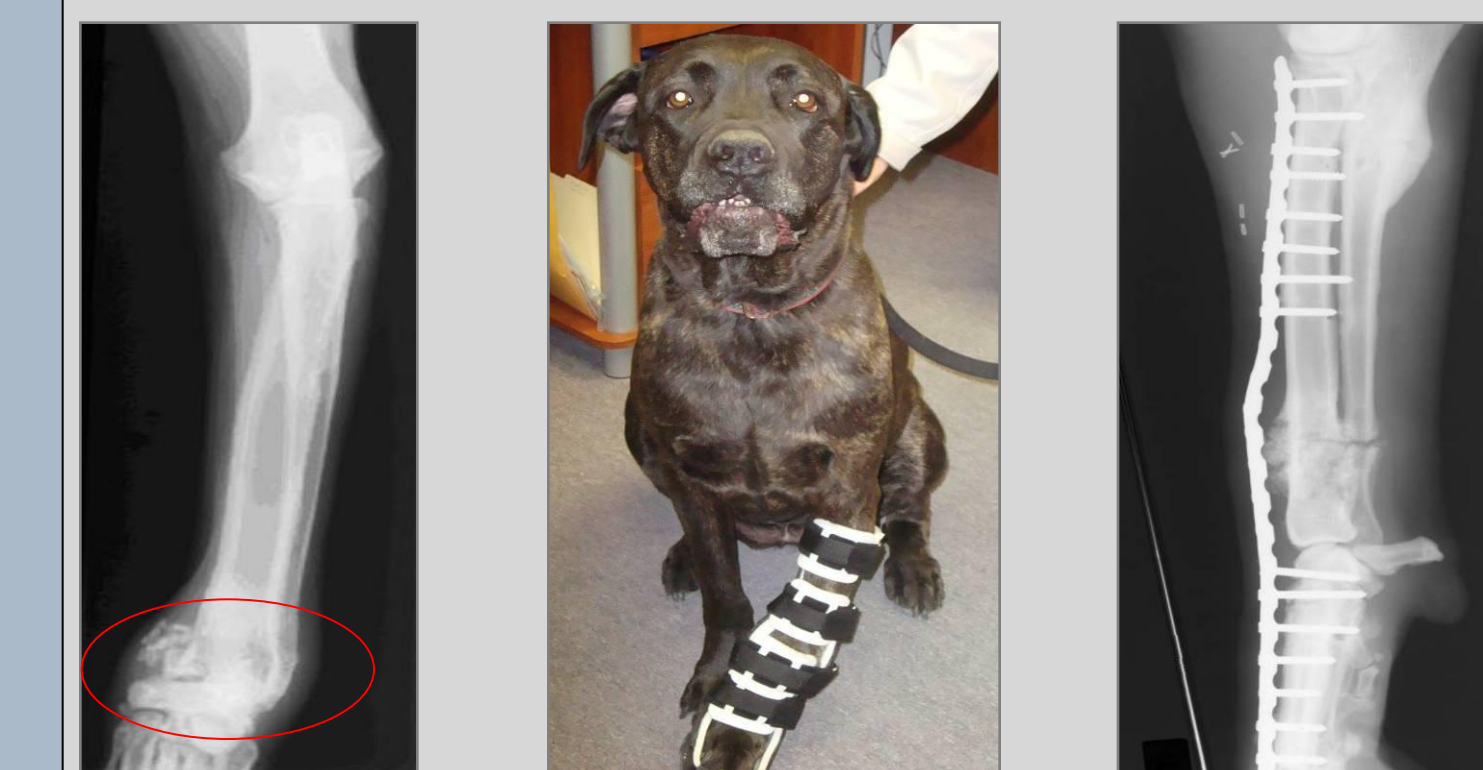
Grade 3 non healing ulcer corresponding to high radiation dose region in patient no. 1.

Grade 1 acute focal moist desquamation. Resolved without therapy with focal region of depigmentation and alopecia.

- ❖ Pathologic fractures: (n = 9)

- 2 fractured before / during SRS
- 5 fractured early (mean of 51 days post SRS)
- 2 fractured late (mean of 325 days post SRS)

Pathologic fractures are the most frequent post SRS complication, and have been managed with amputation (n = 3), surgical stabilization (n = 2) or external coaptation (n = 4).



(Left) Pathologic fracture  
(Center) External support  
(Right) Surgical stabilization

### Conclusions

❖ SRS provides excellent local tumor control and durable pain palliation, thus expanding our non-surgical local control options for OSA.

❖ Pathologic fracture is the most common complication.

❖ Acute radiation side effects are mild and focal when 0.5% skin radiation dose is ≤ 35Gy.

❖ Survival time is equivalent to standard of care therapy for patients with longer follow-up times.

❖ A variety of anatomic sites can be treated, expanding our available limb salvage options.

❖ Future goals include using force plate gait analysis to objectively measure gait changes, creating fracture prediction models and developing bone regenerative strategies.

### References

1. Farese, J.P., et al., Stereotactic radiosurgery for treatment of osteosarcomas involving the distal portions of the limbs in dogs. J Am Vet Med Assoc, 2004, 225(10): p. 1567-72, 1548.