Osteoblastoma vs Osteo-blastoma-like Osteosarcoma

XXXII Congress of the International Academy of Pathology

Bone Pathology - Mimics of Malignancy: an emphasis on microscopic features and best use of limited molecular tests

Daniel Baumhoer, Bone Tumour Reference Centre, Basel, Switzerland

Amman, October 15th, 2018

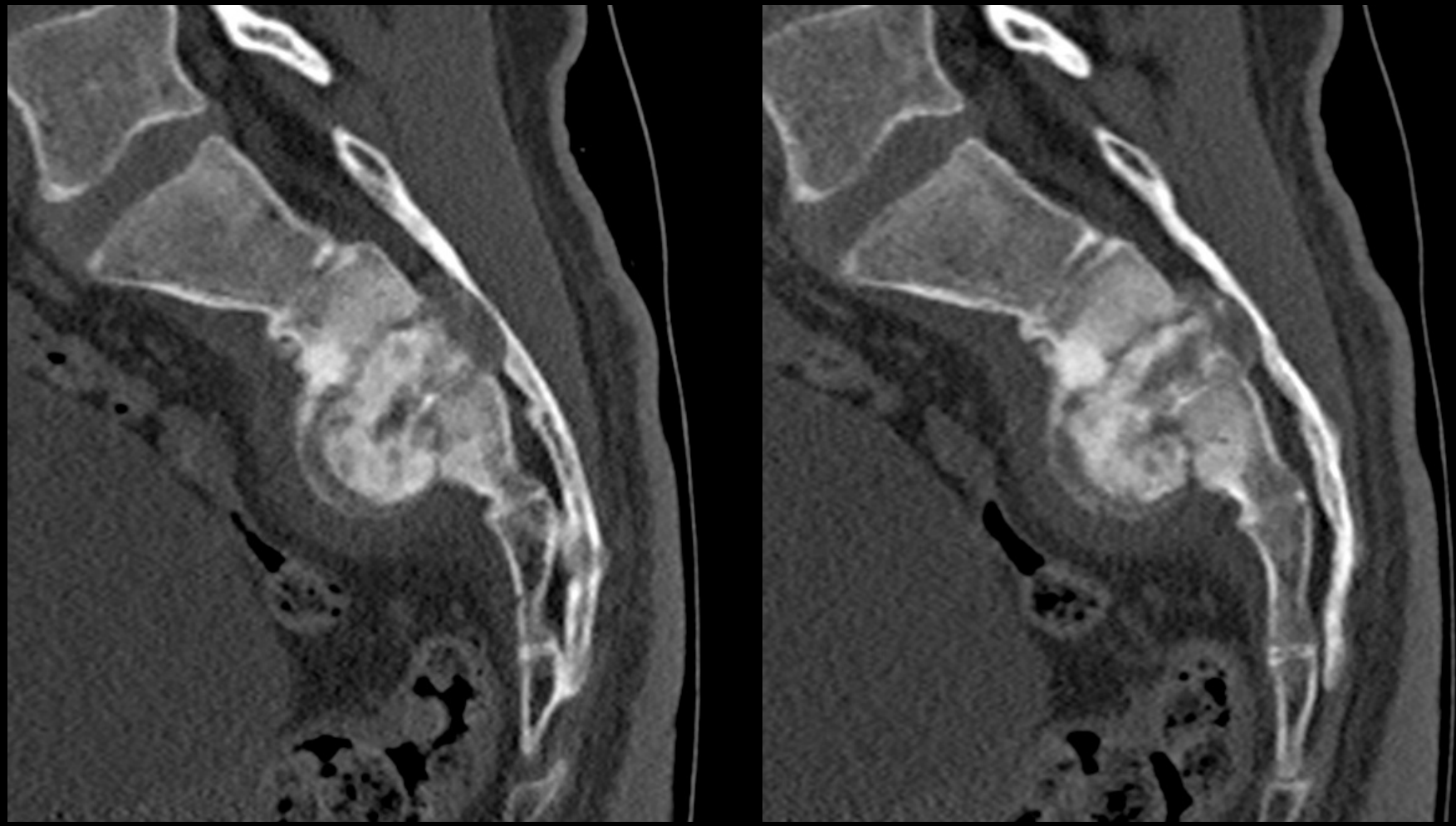
University Hospital Basel

BTRC

Case #1

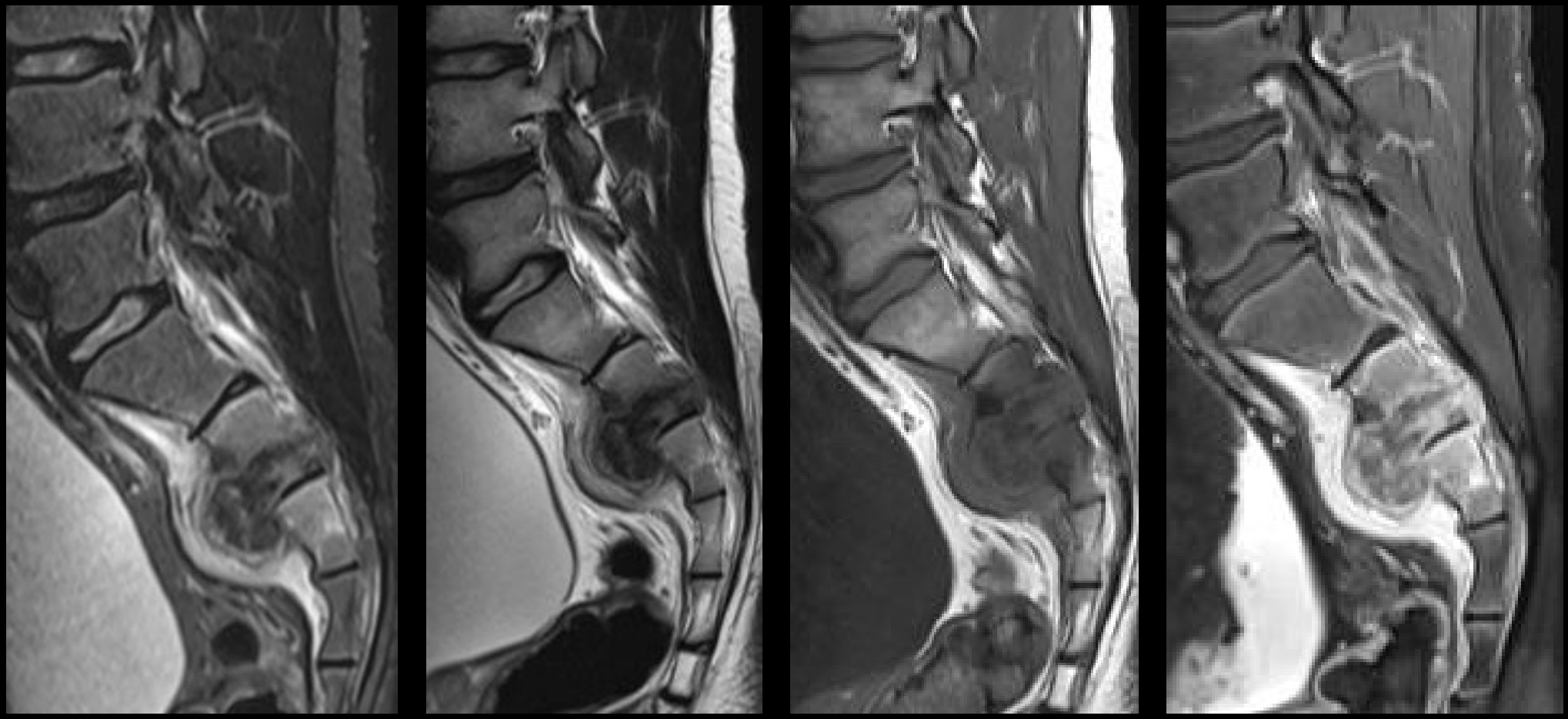
17-year old boy with lower back pain since 12 months after an accident during a judo fight; no relief after consulting a chiropractic, no fever, no B-symptoms

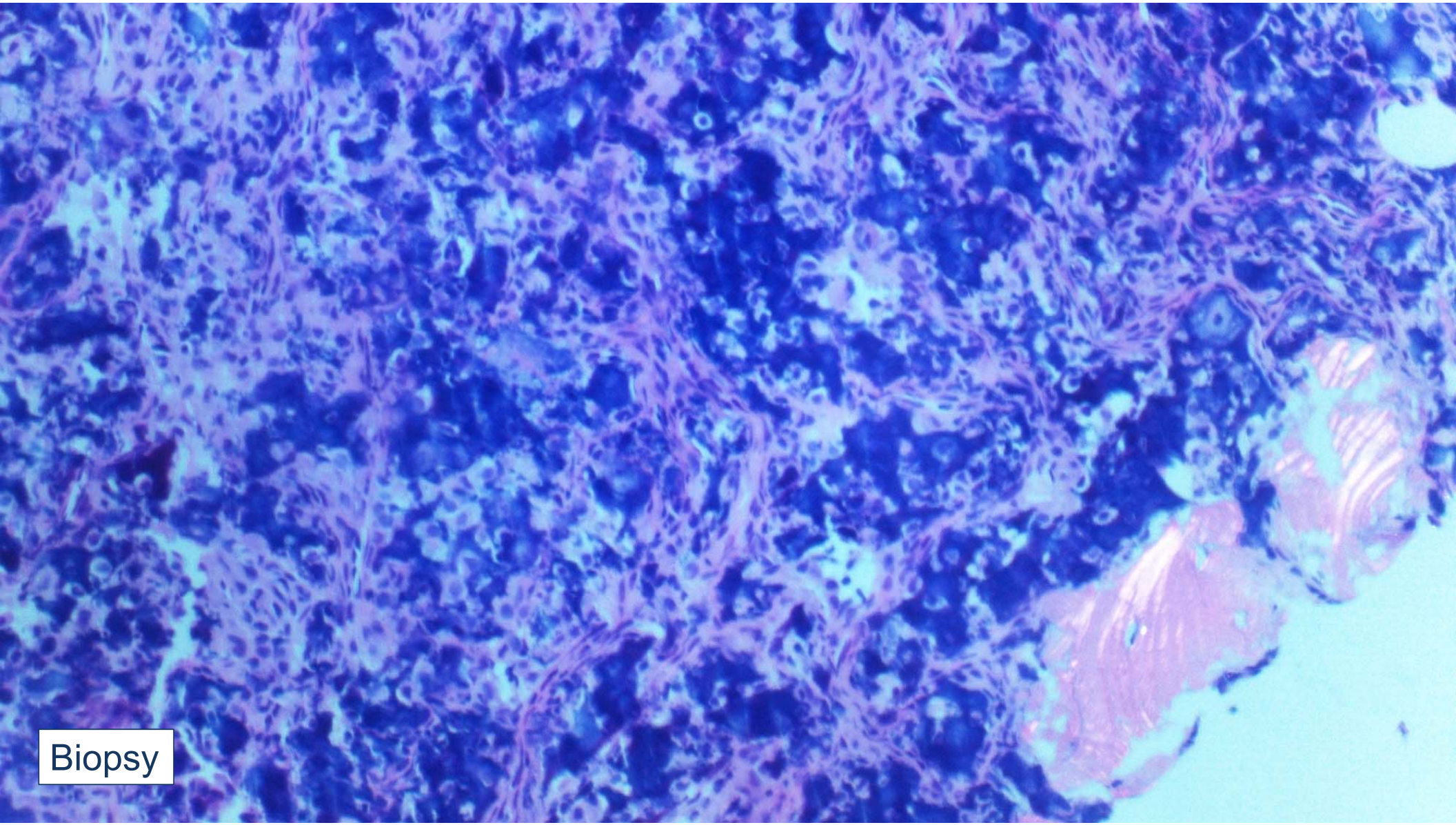
Sagittal reformation of a non-enhanced CT of the sacrum

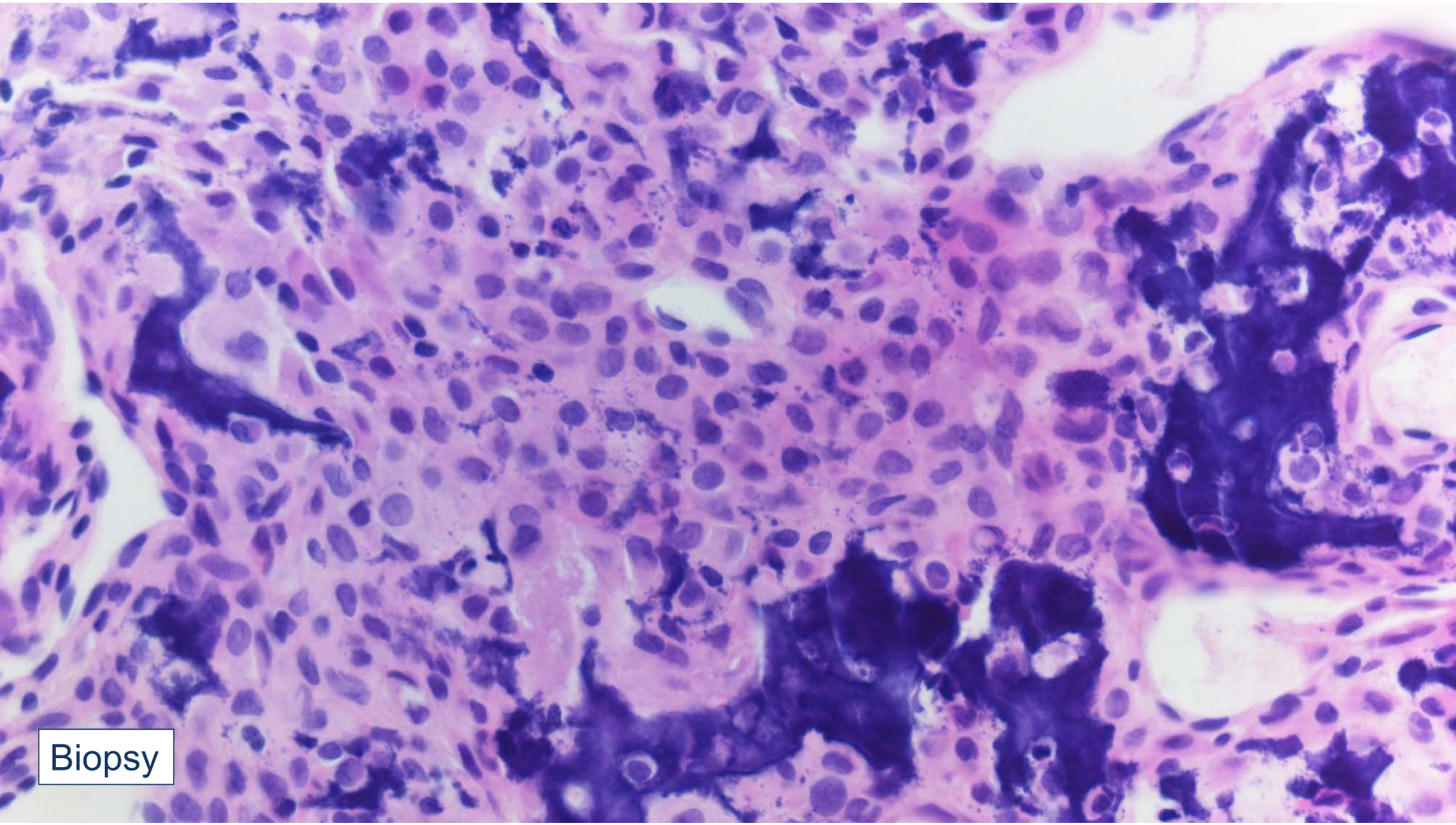


MRI of the lumbosacral spine: sagittal images

TIRM | T2 | T1 | T1 FS contrast-enhanced

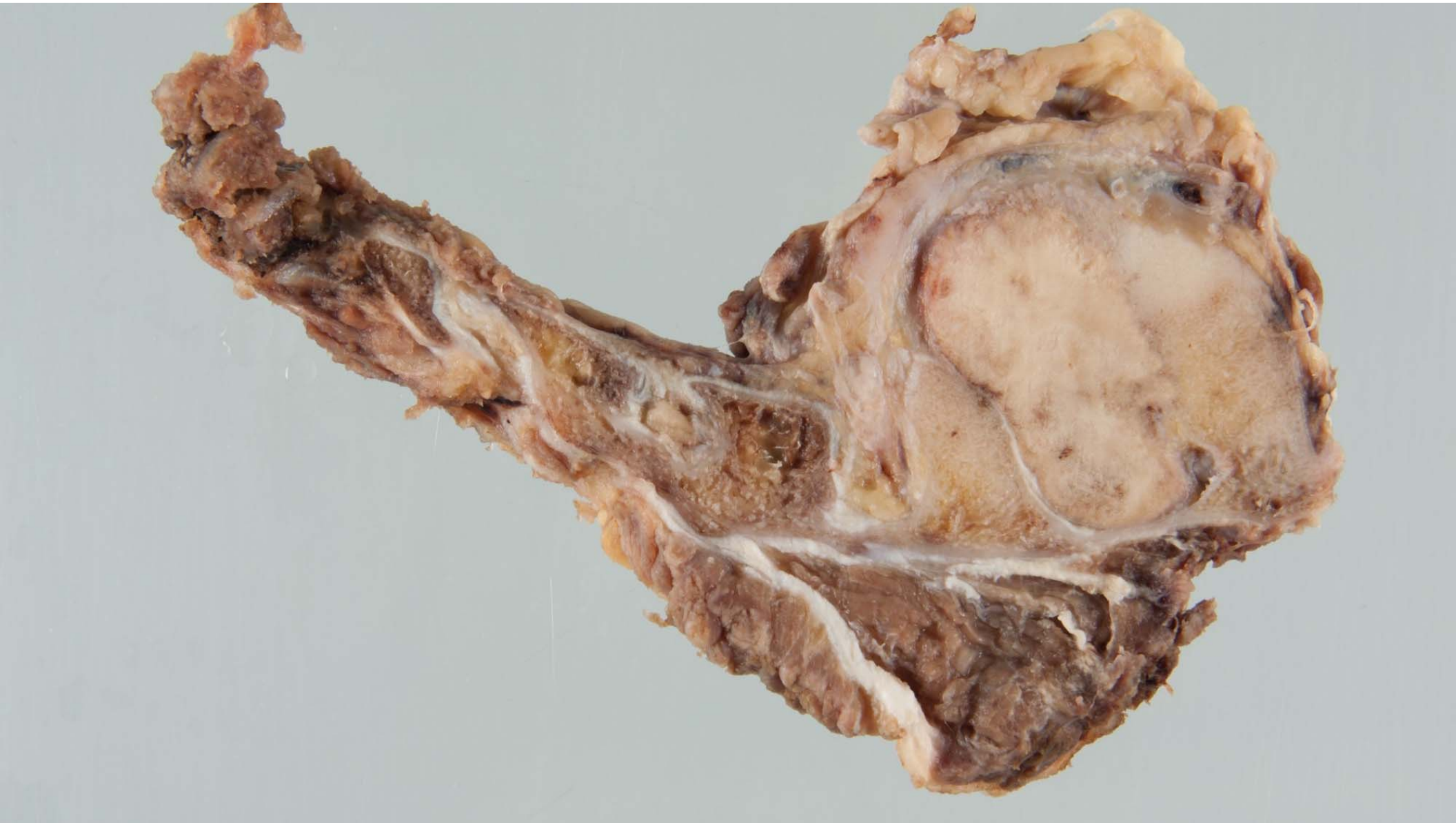


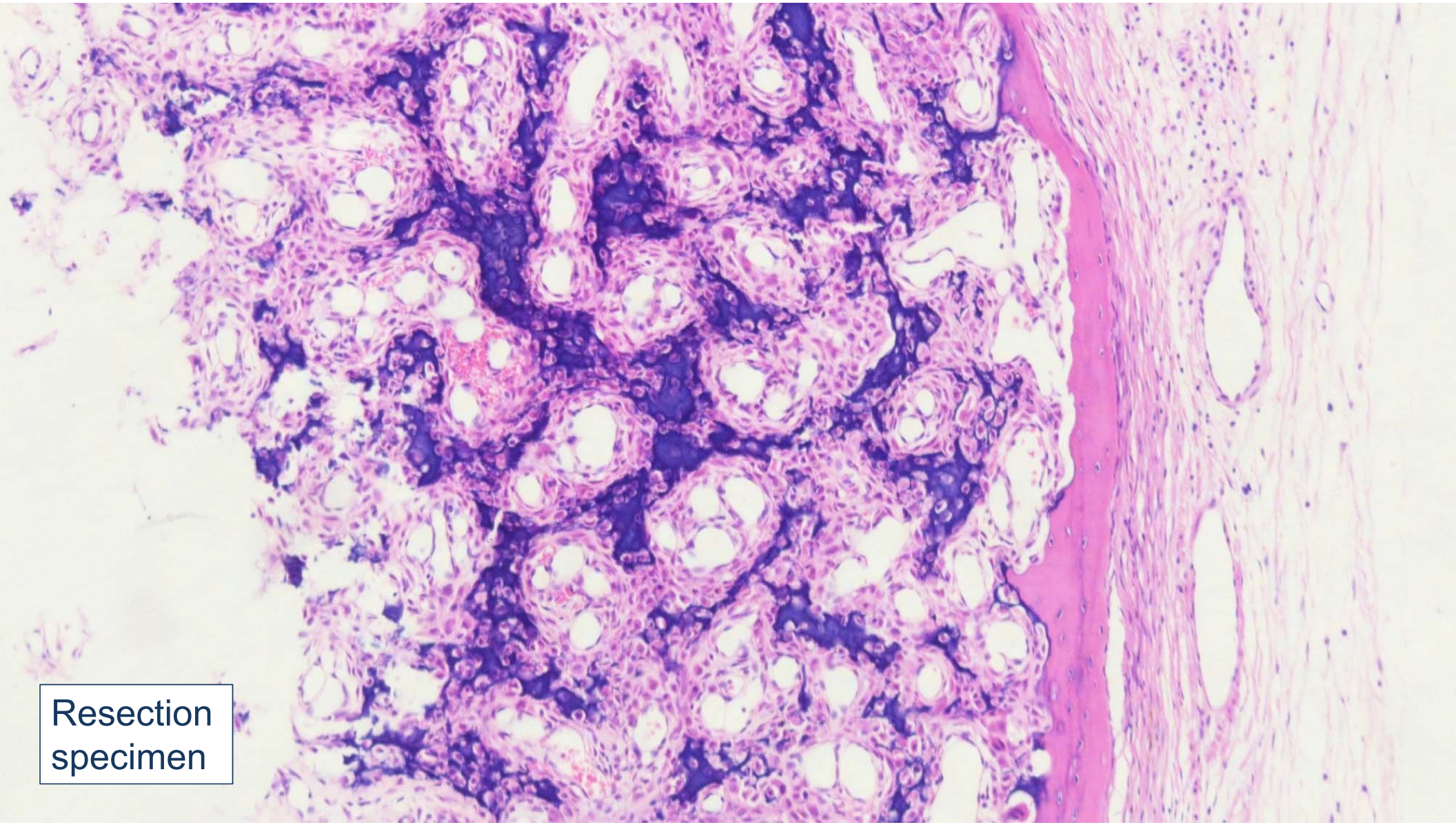

Biopsy

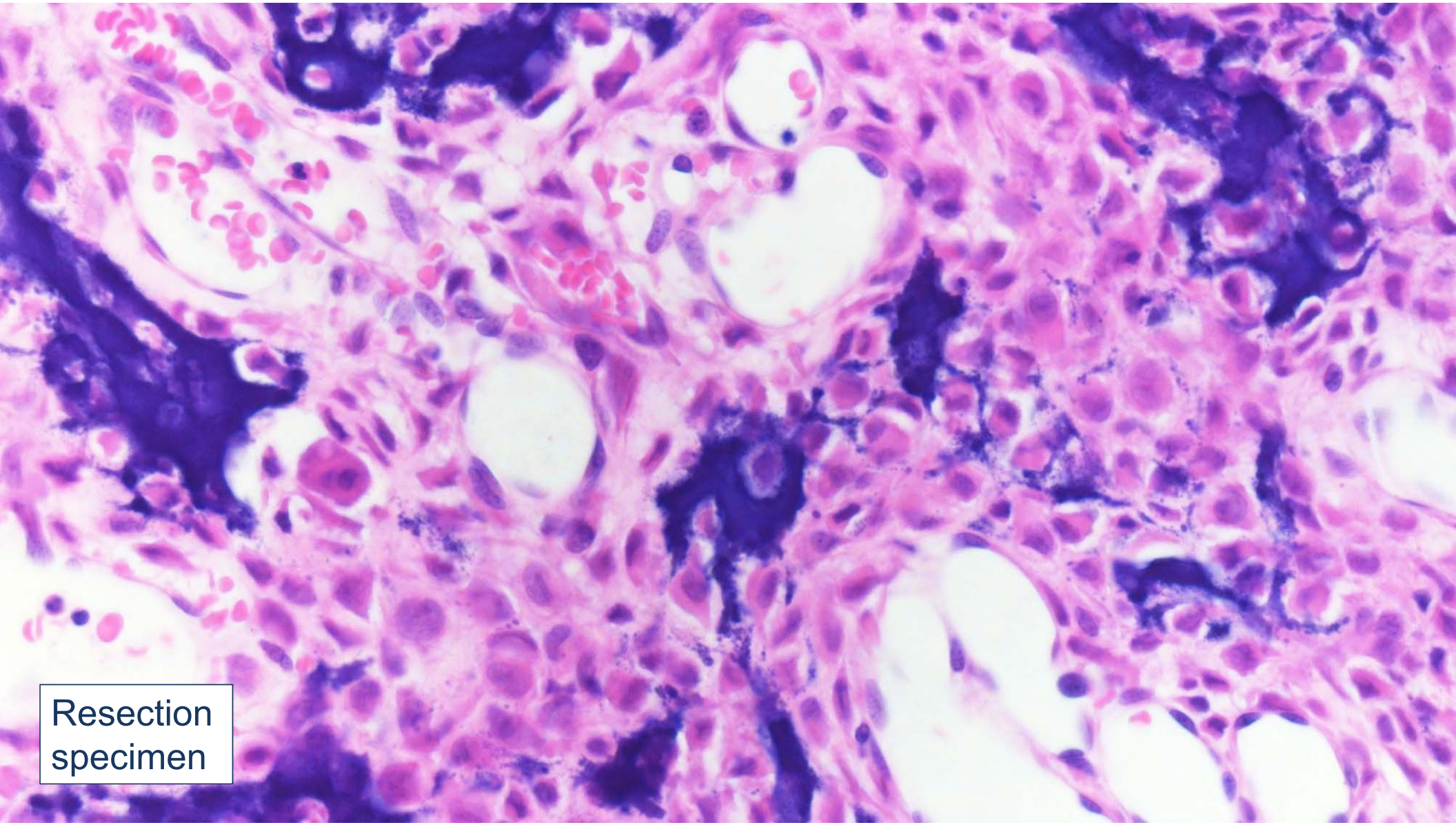

Biopsy

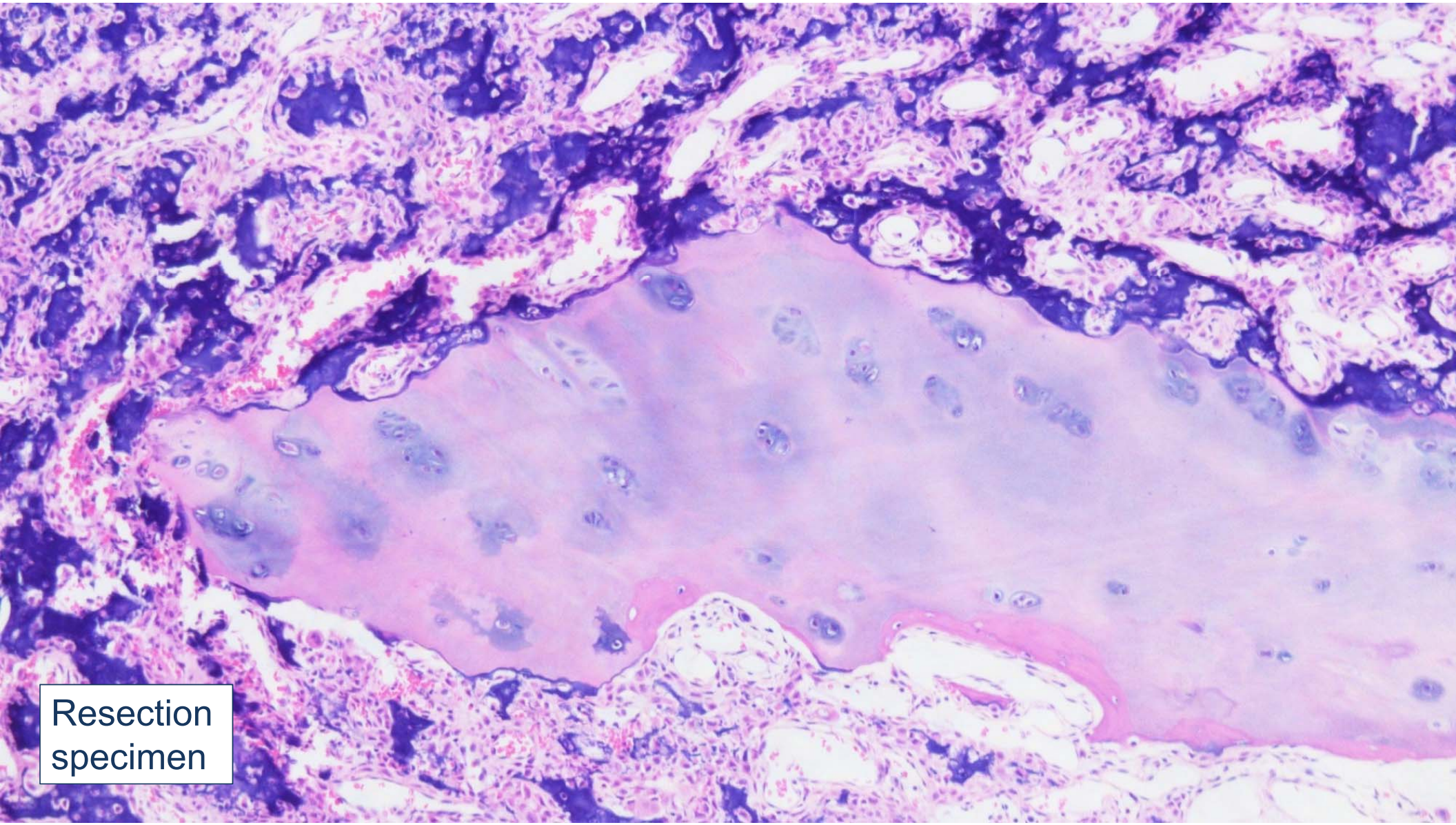
OB

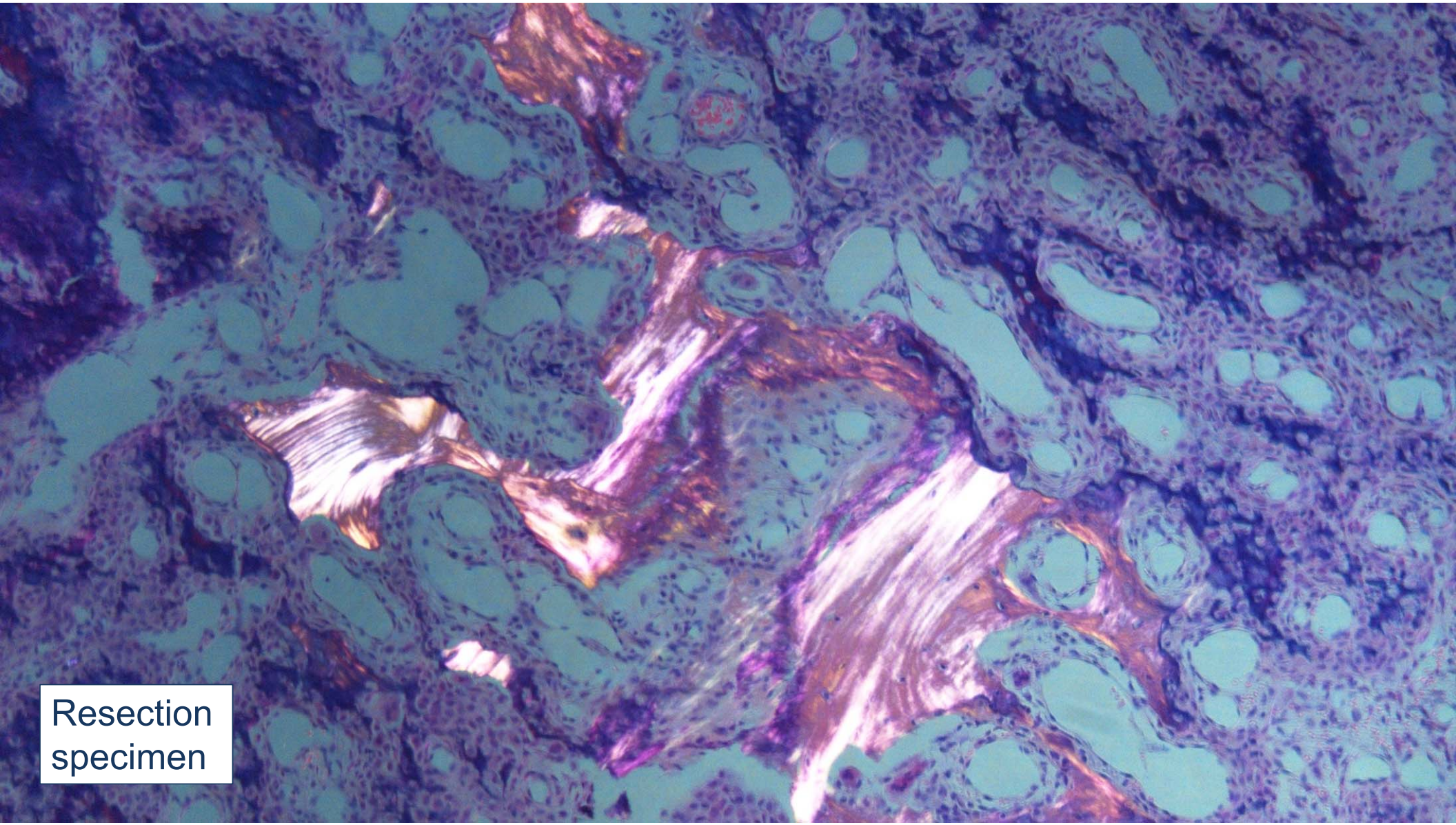
OS




Resection
specimen


Resection
specimen

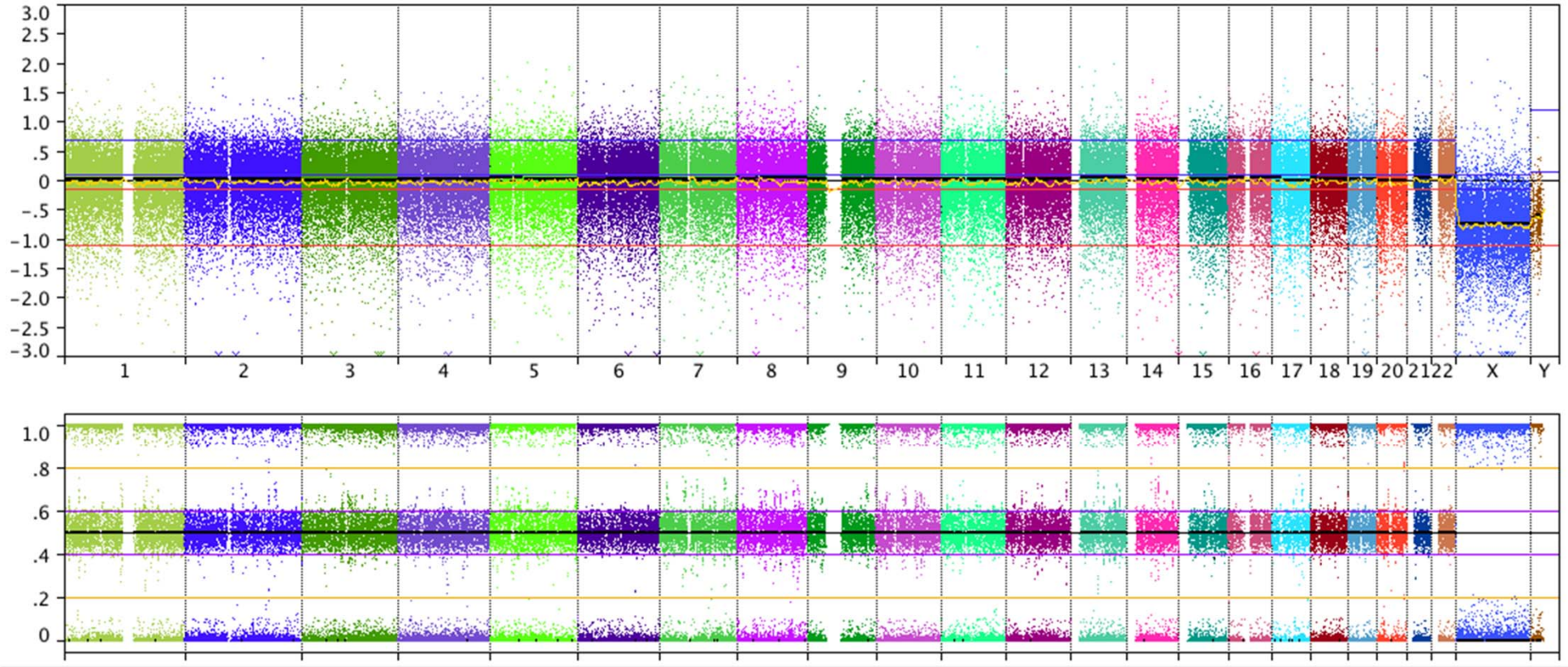

Resection
specimen


Resection
specimen

OB-like Osteosarcoma
No response to Cx-Th
Clear margins (R0)

OncoScan Array

log R ratios (CNs)



B-allele frequencies (LOH)

nature COMMUNICATIONS

ARTICLE

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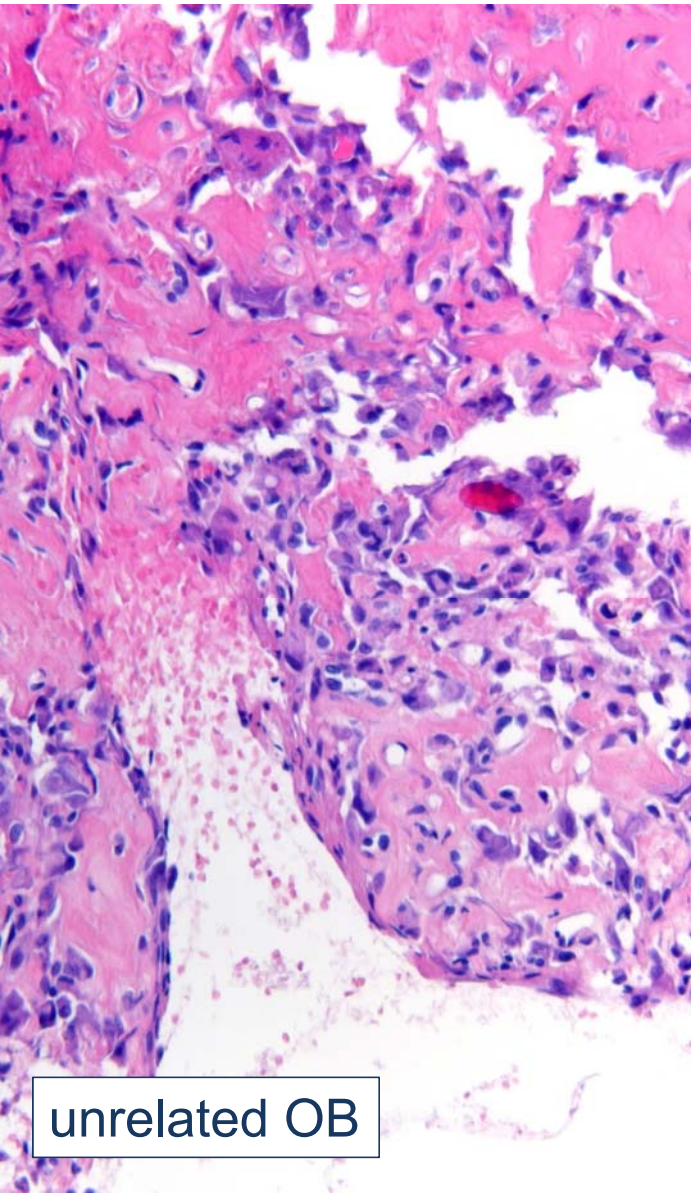
Recurrent rearrangements of *FOS* and *FOSB* define osteoblastoma

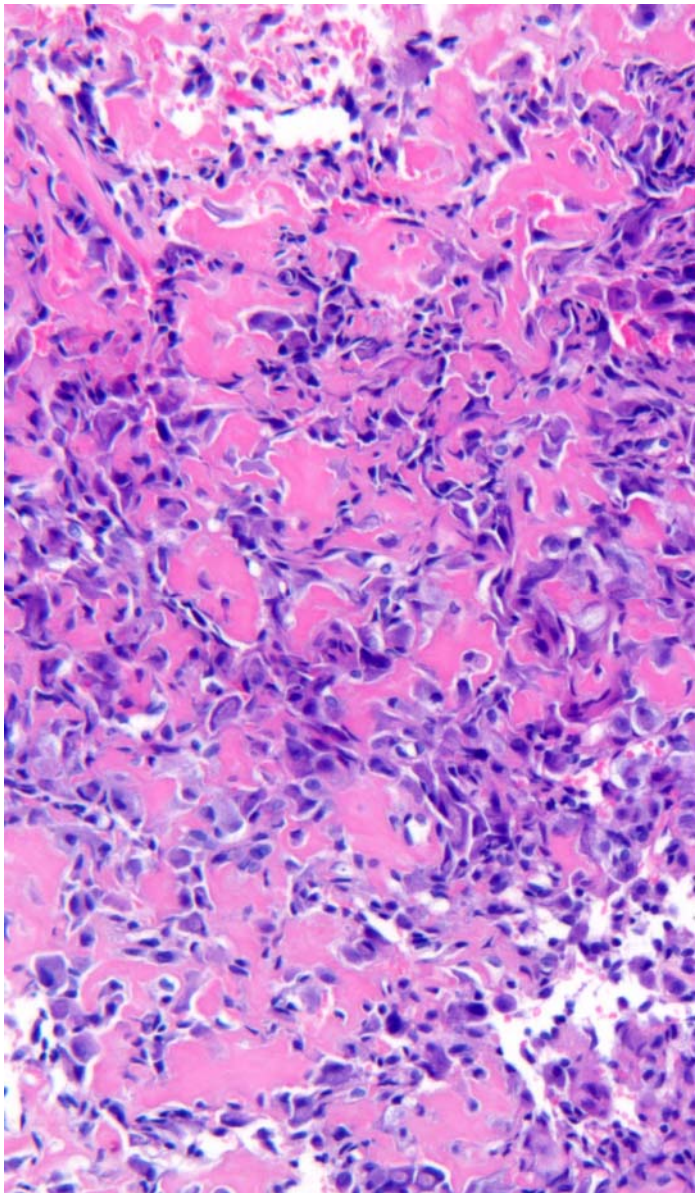
Matthew W. Fittall[1,2,3], William Mifsud[2,3,4], Nischalan Pillay[2,5], Hongtao Ye[5], Anna-Christina Strobl[5], Annelien Verfaillie[1], Jonas Demeulemeester[1,6], Lei Zhang[7], Fitim Berisha[5], Maxime Tarabichi[1,3], Matthew D. Young[3], Elena Miranda[2], Patrick S. Tarpey[3], Roberto Tirabosco[5], Fernanda Amary[5], Agamemnon E. Grigoriadis[8], Michael R. Stratton[3], Peter Van Loo[1,6], Cristina R. Antonescu[7], Peter J. Campbell[3], Adrienne M. Flanagan[2,5] & Sam Behjati[3,9]

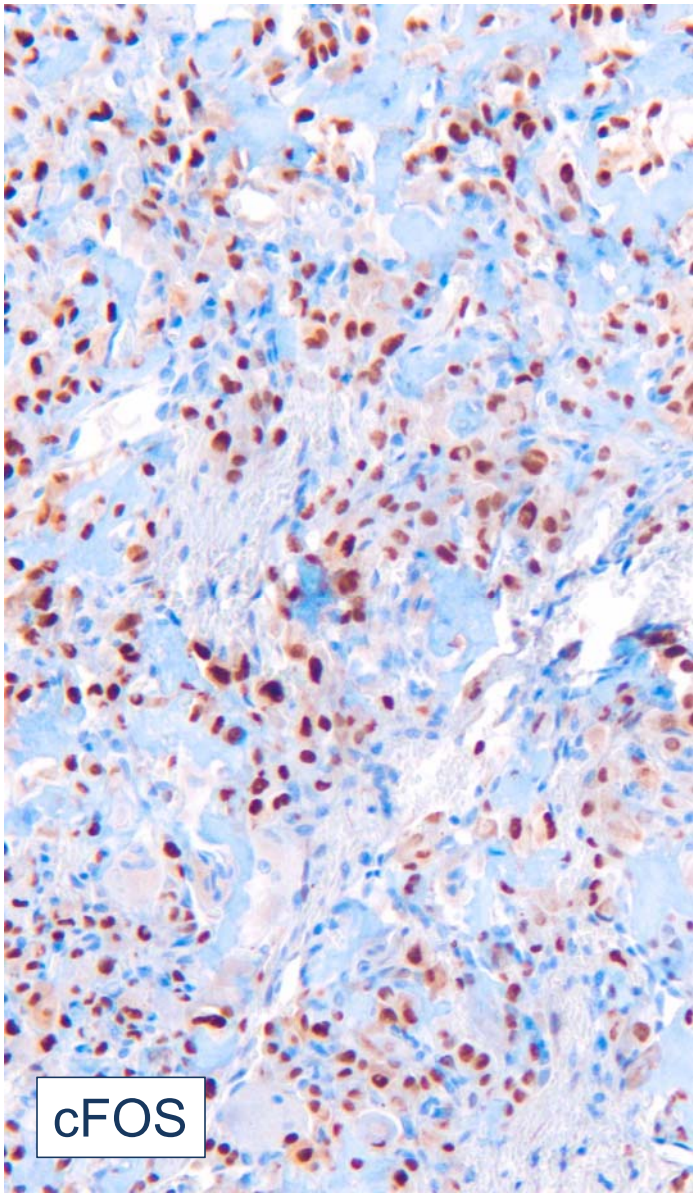
The transcription factor *FOS* has long been implicated in the pathogenesis of bone tumours, following the discovery that the viral homologue, *v-fos*, caused osteosarcoma in laboratory mice. However, mutations of *FOS* have not been found in human bone-forming tumours. Here, we report recurrent rearrangement of *FOS* and its paralogue, *FOSB*, in the most common benign tumours of bone, osteoblastoma and osteoid osteoma. Combining whole-genome DNA and RNA sequences, we find rearrangement of *FOS* in five tumours and of *FOSB* in one tumour. Extending our findings into a cohort of 55 cases, using FISH and immunohistochemistry, provide evidence of ubiquitous mutation of *FOS* or *FOSB* in osteoblastoma and osteoid osteoma. Overall, our findings reveal a human bone tumour defined by mutations of *FOS* and *FOSB*.

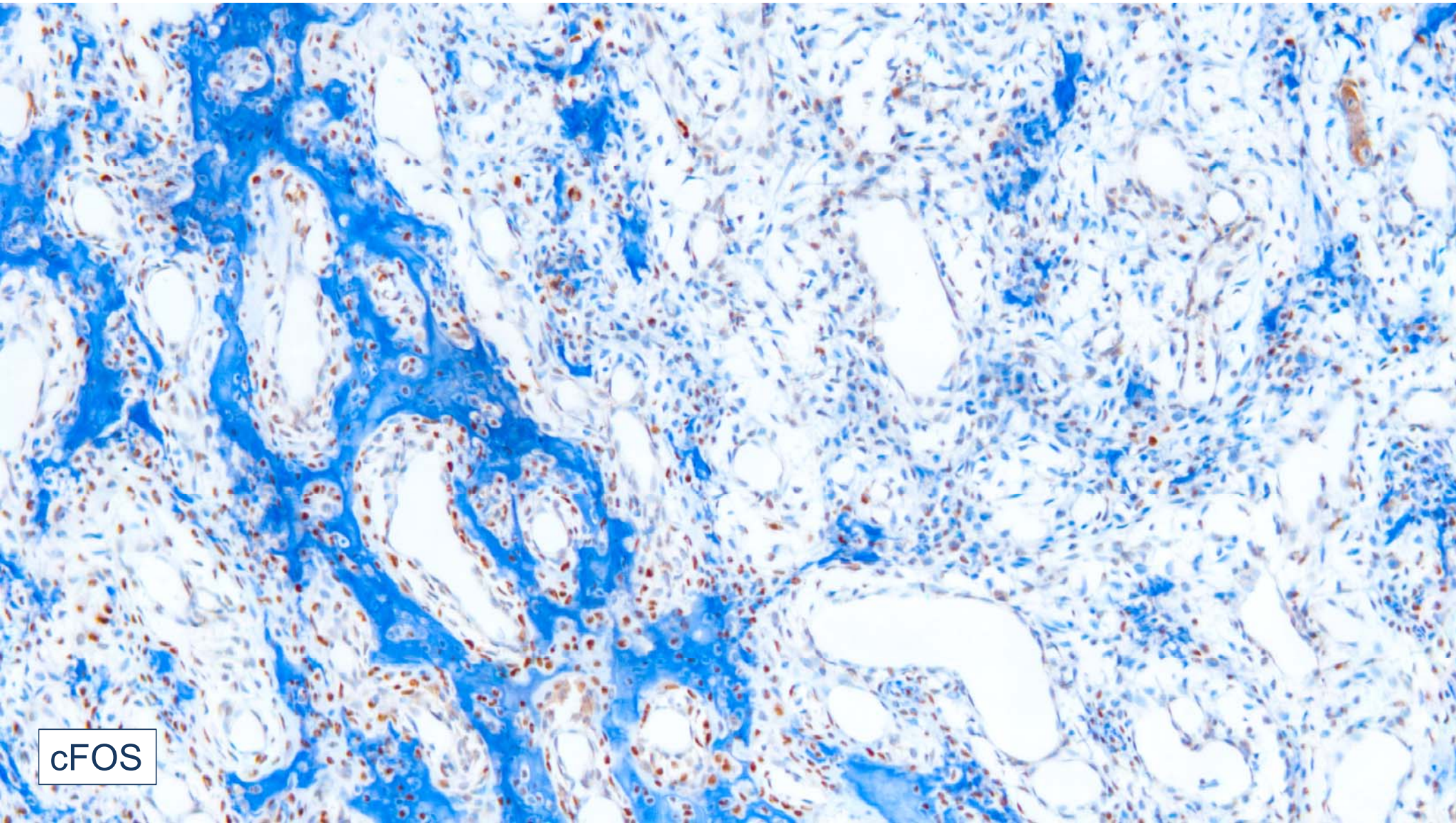
***FOS* and *FOSB* alterations are ubiquitous in osteoblastoma**. To validate our findings, we examined by fluorescence in situ hybridisation (FISH) an extension cohort of 55 formalin-fixed paraffin-embedded (FFPE) histologically typical cases of osteoblastoma and osteoid osteoma (Supplementary Data 1). In these 55 samples, we found *FOSB* and *FOS* breakapart signals in 1 and 48 tumours, respectively (89% in total; Supplementary Data 1).

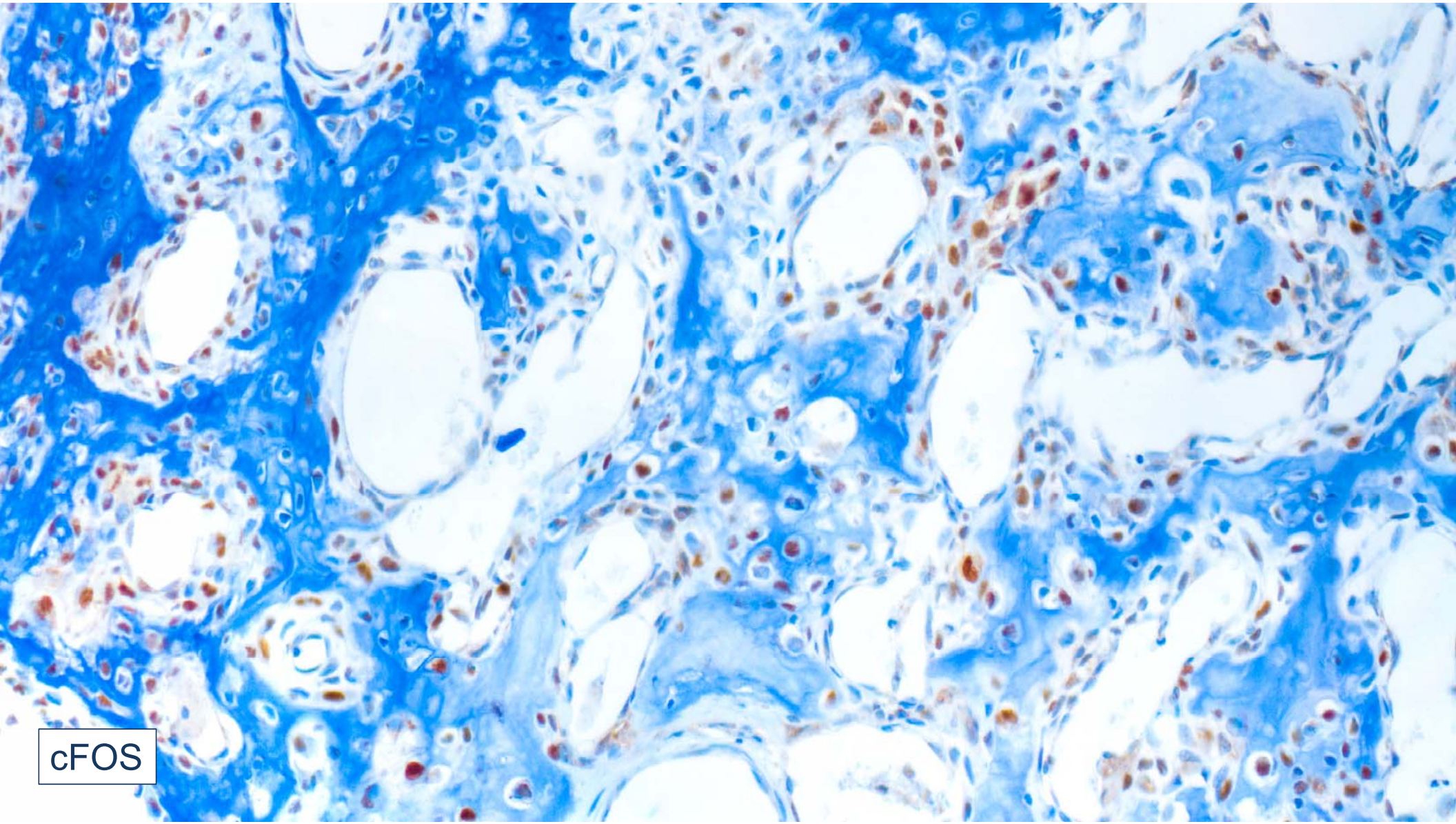
We speculated that the six FISH-negative cases may also harbour *FOS* or *FOSB* rearrangements that were not detected because FISH analysis is hampered in tumours of low cellularity, a frequent feature of osteoblastoma[1]. FISH may also miss cases with short distance intrachromosomal rearrangements, such as tandem duplications, that insufficiently separate probe target sequences. Since sufficient tissue was available for 3/6 negative cases, we sought alternative evidence for *FOS* dysregulation by immunohistochemistry. All three samples demonstrated strong nuclear FOS immunoreactivity, supporting the notion that alterations in *FOS* or *FOSB* underpin every case of osteoblastoma and osteoid osteoma (Supplementary Fig. 4b). FOSB immunohistochemistry was uninformative in osteoblastoma, consistent with previous experience with decalcified tumours (Supplementary Fig. 4c)[9].


unrelated OB




cFOS

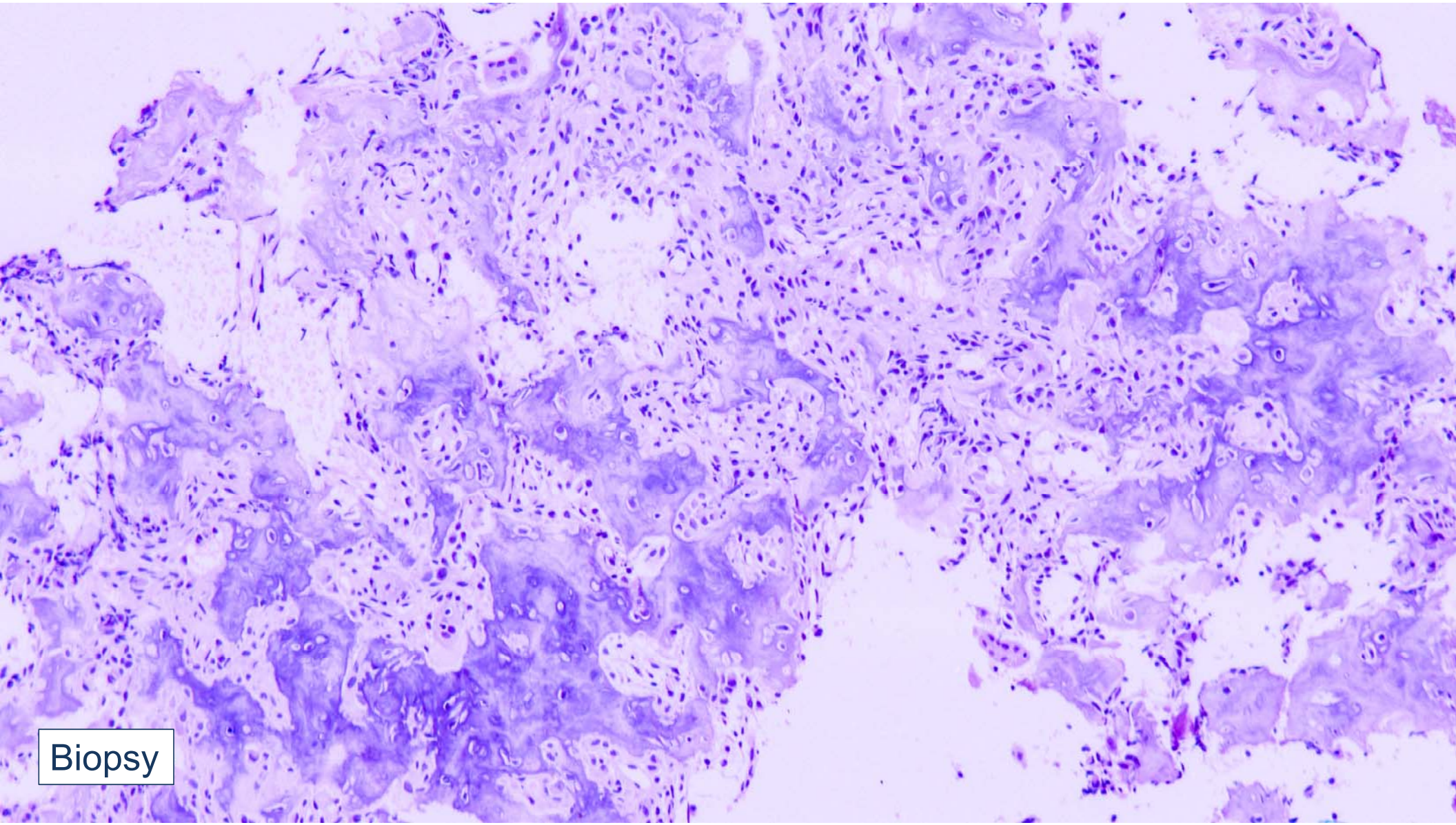

cFOS

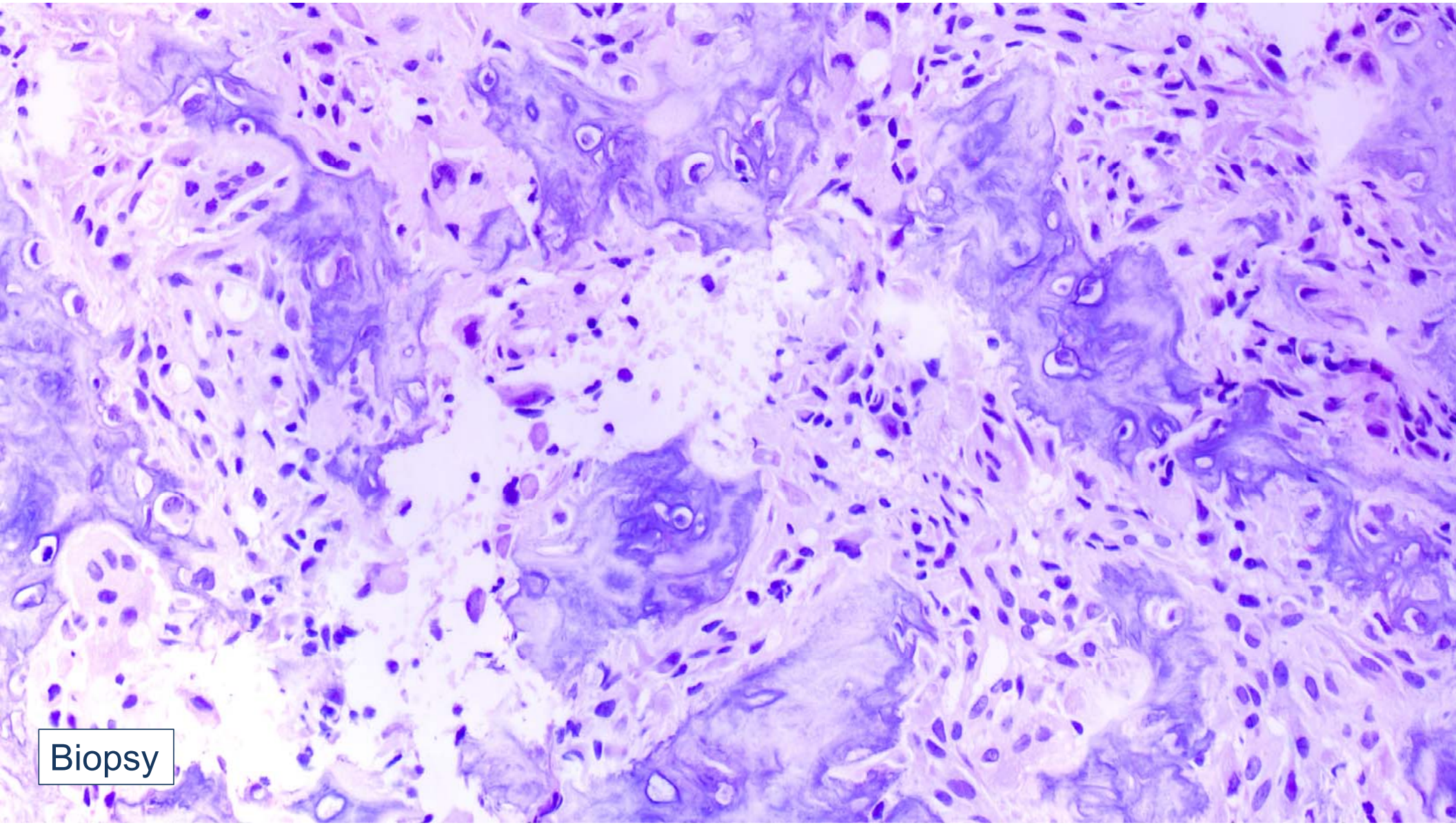

cFOS

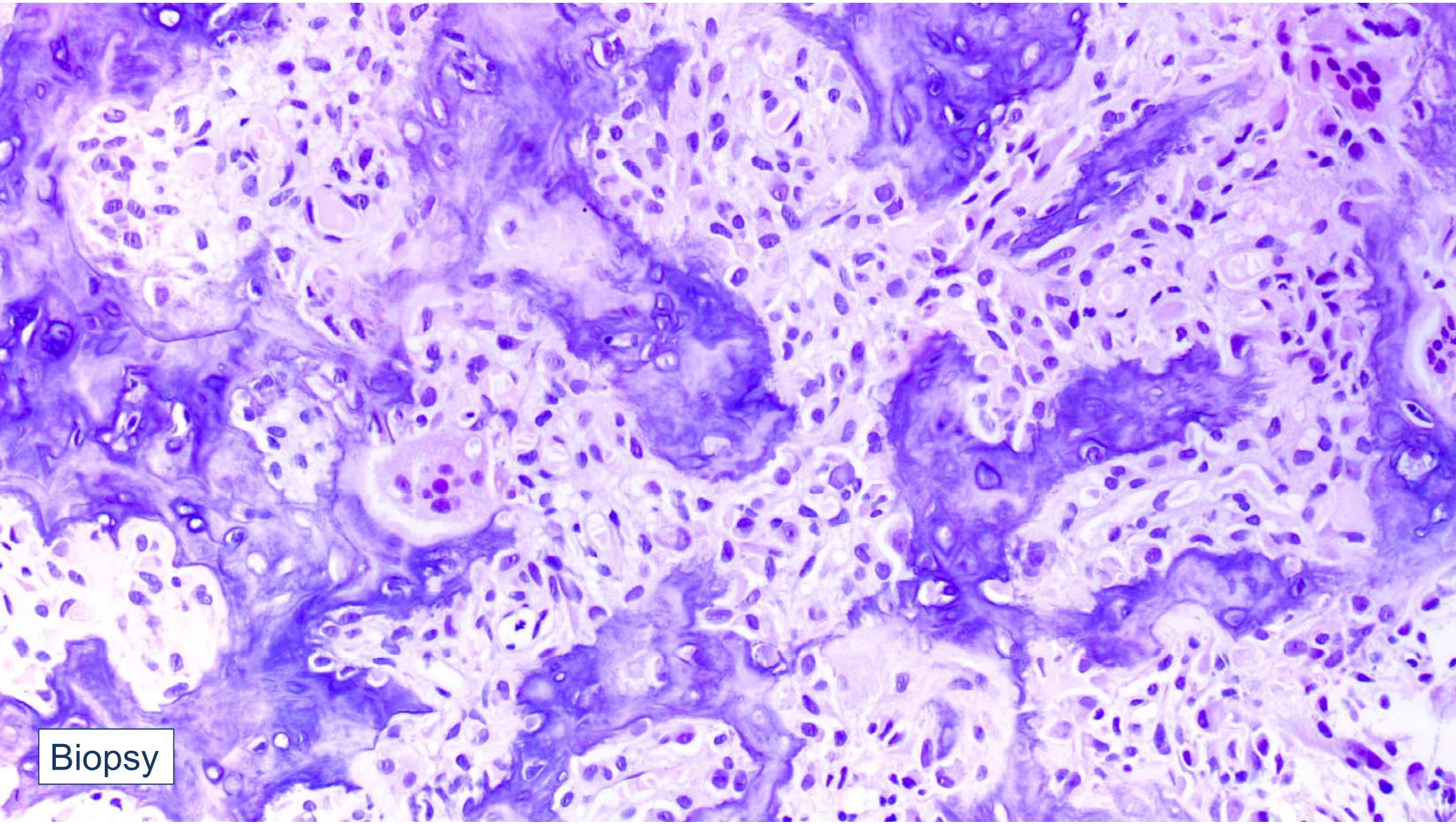
Case #2

24-year old woman with increasing tenderness during mastification and on percussion, palbable protrusion, regio 46

Digital volume tomography (DVT)


Biopsy

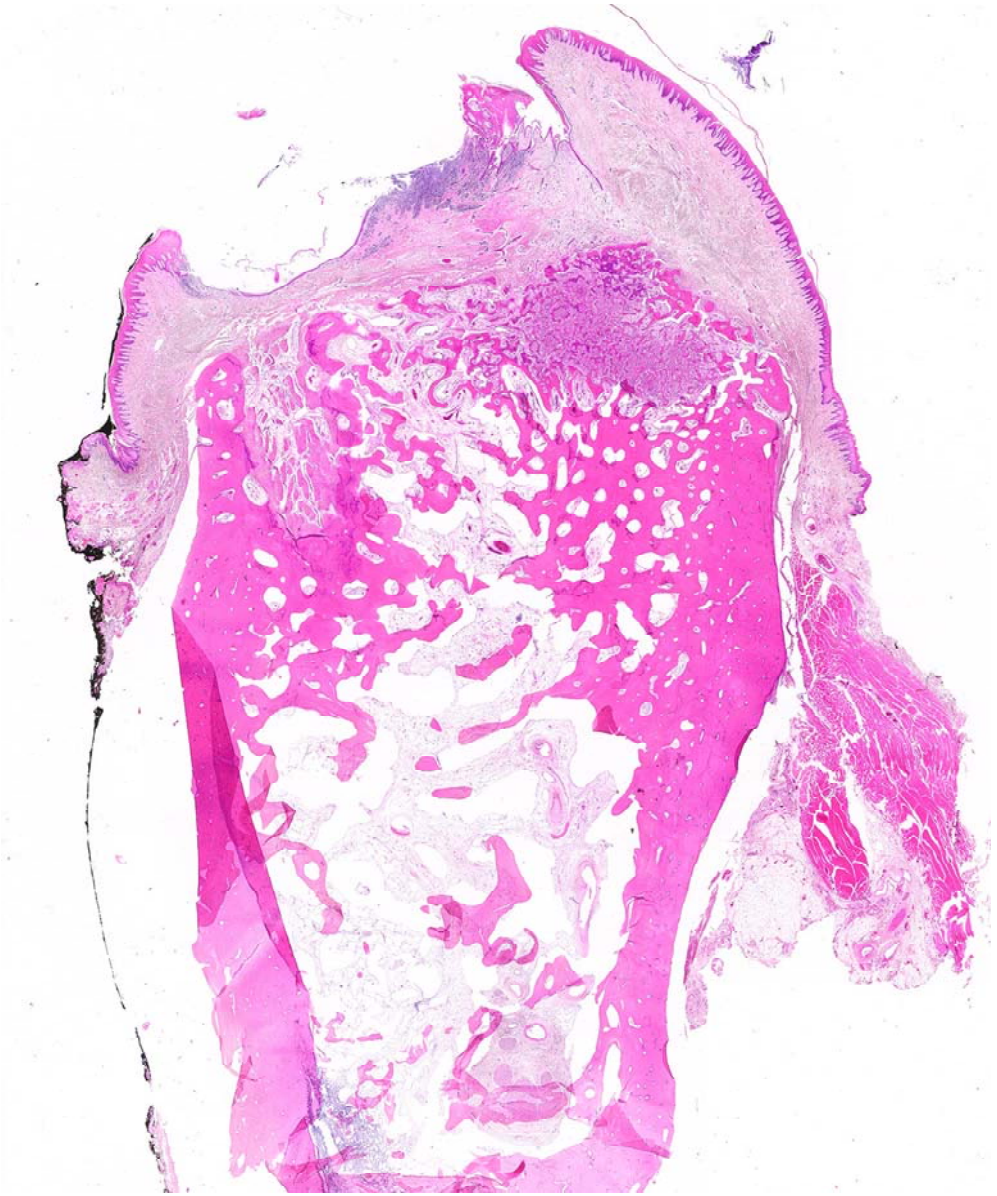

Biopsy


Biopsy

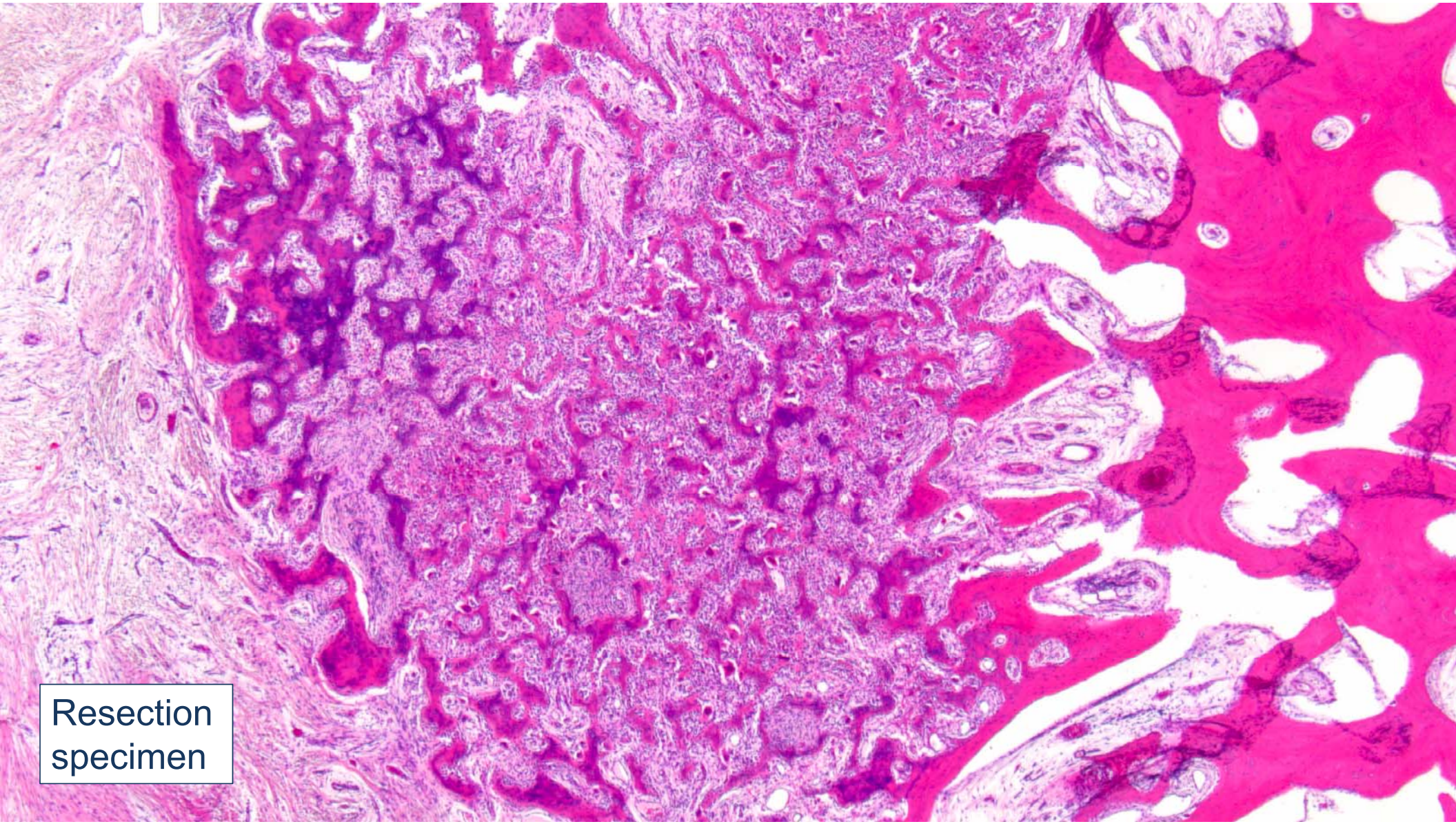
OO

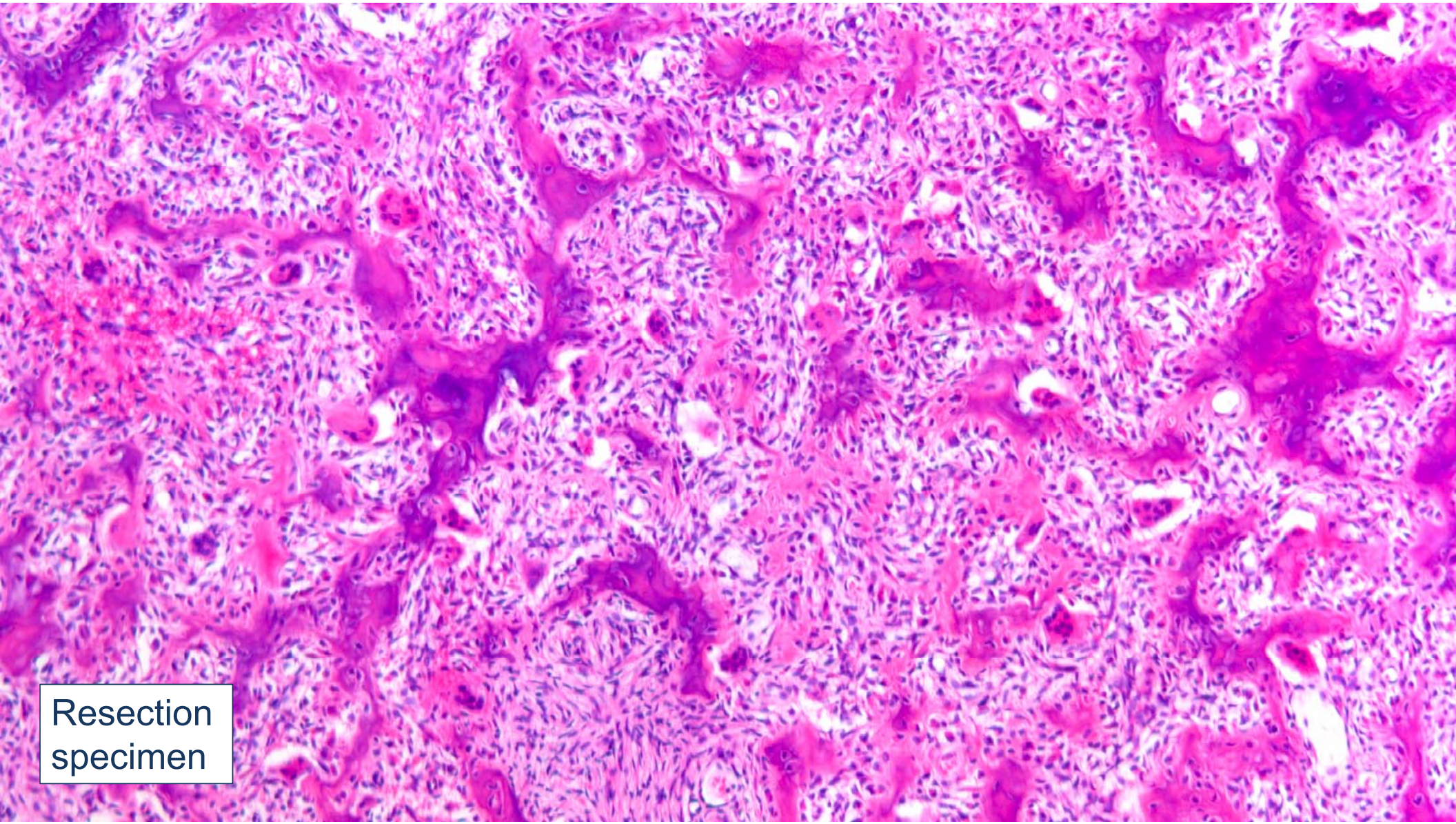
?

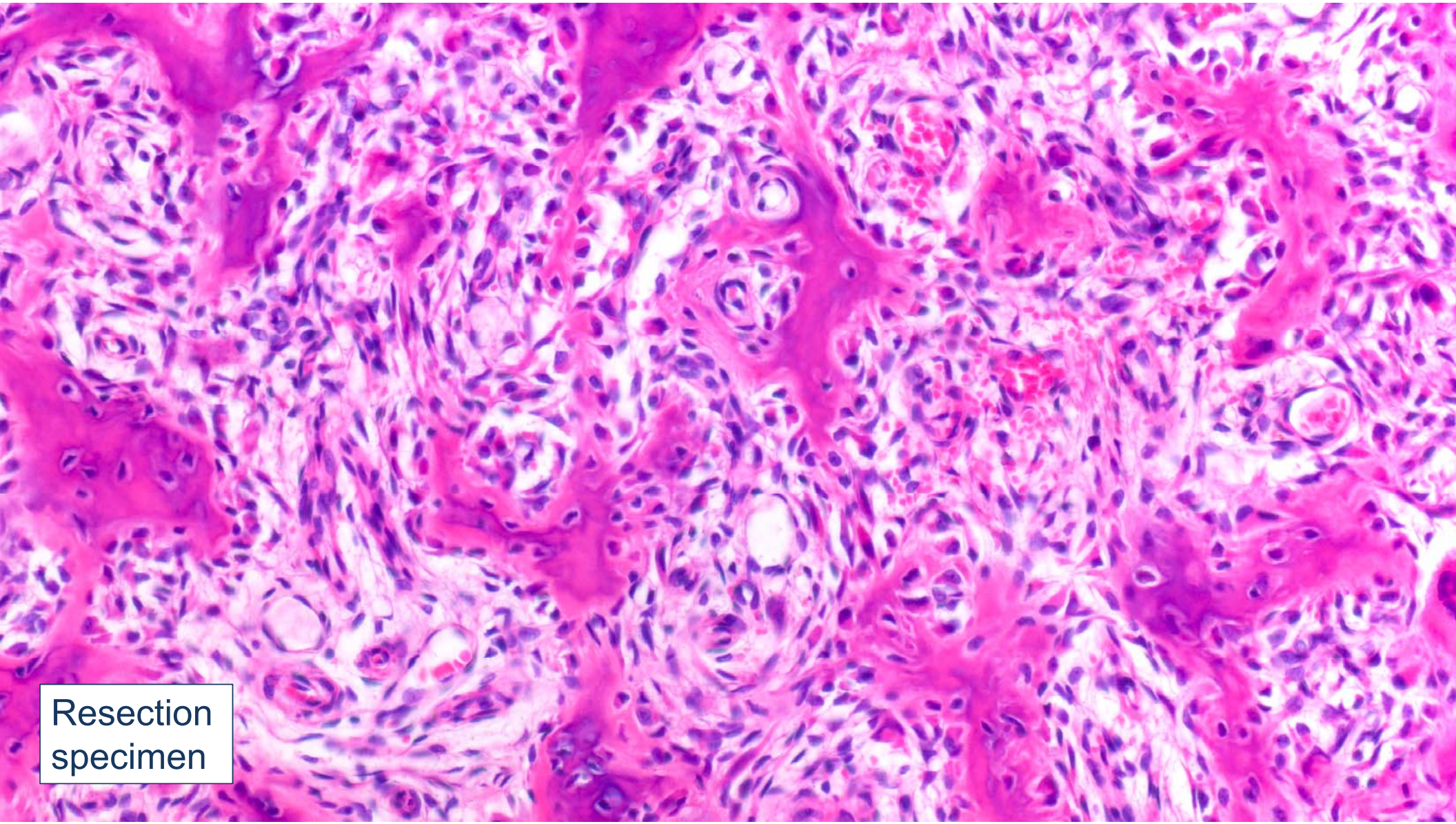
OS



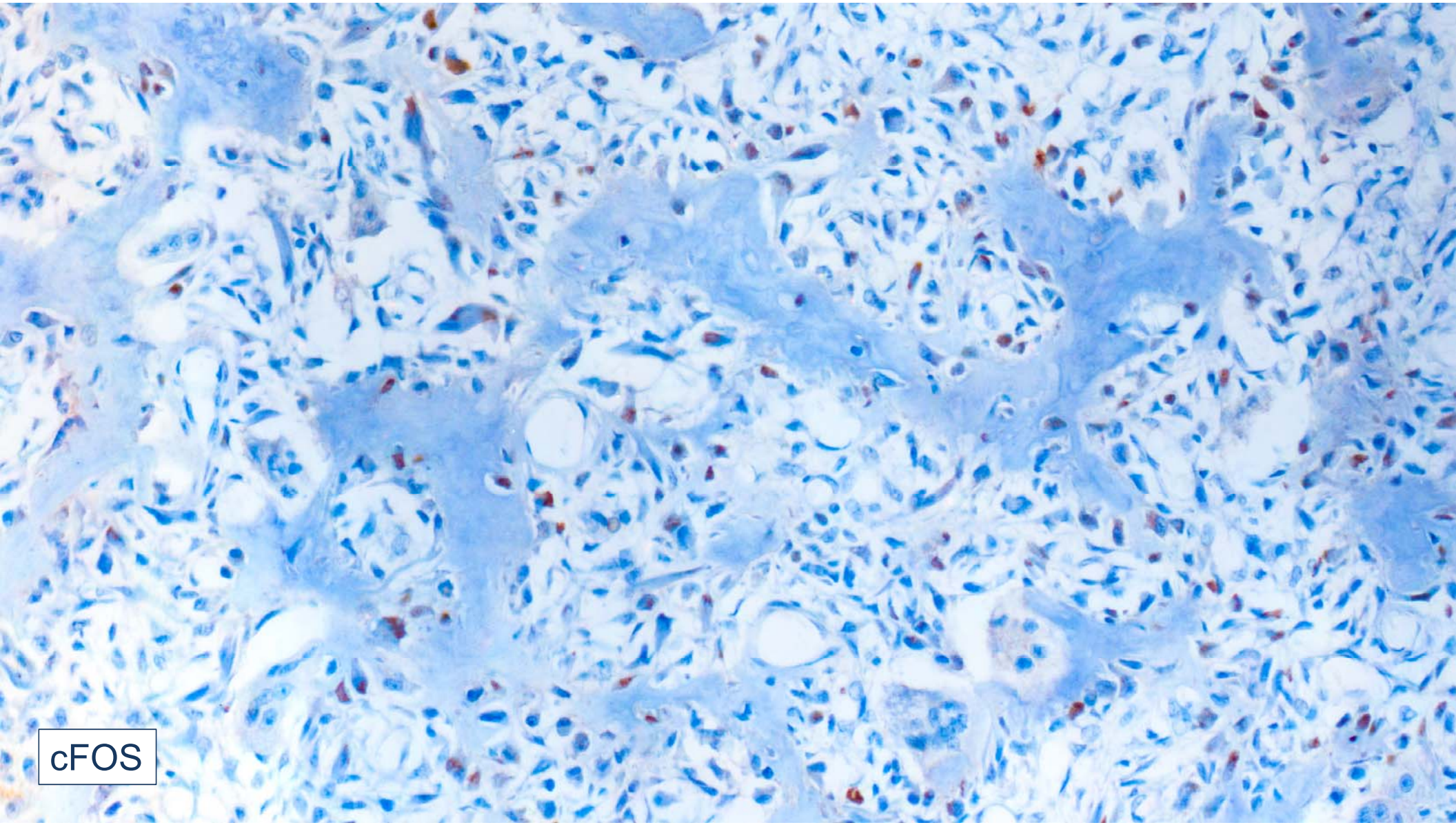
Resection specimen

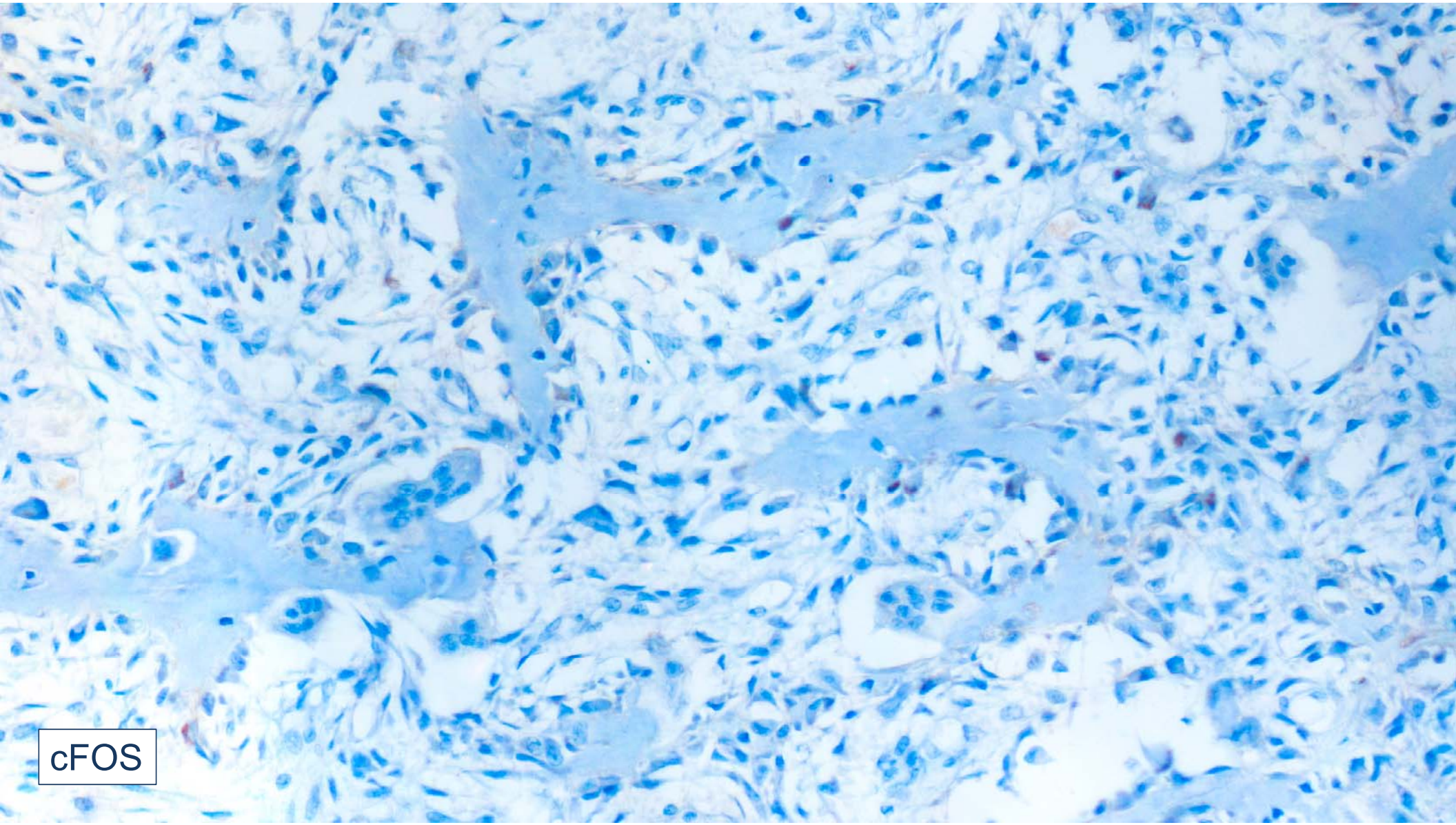

Resection
specimen

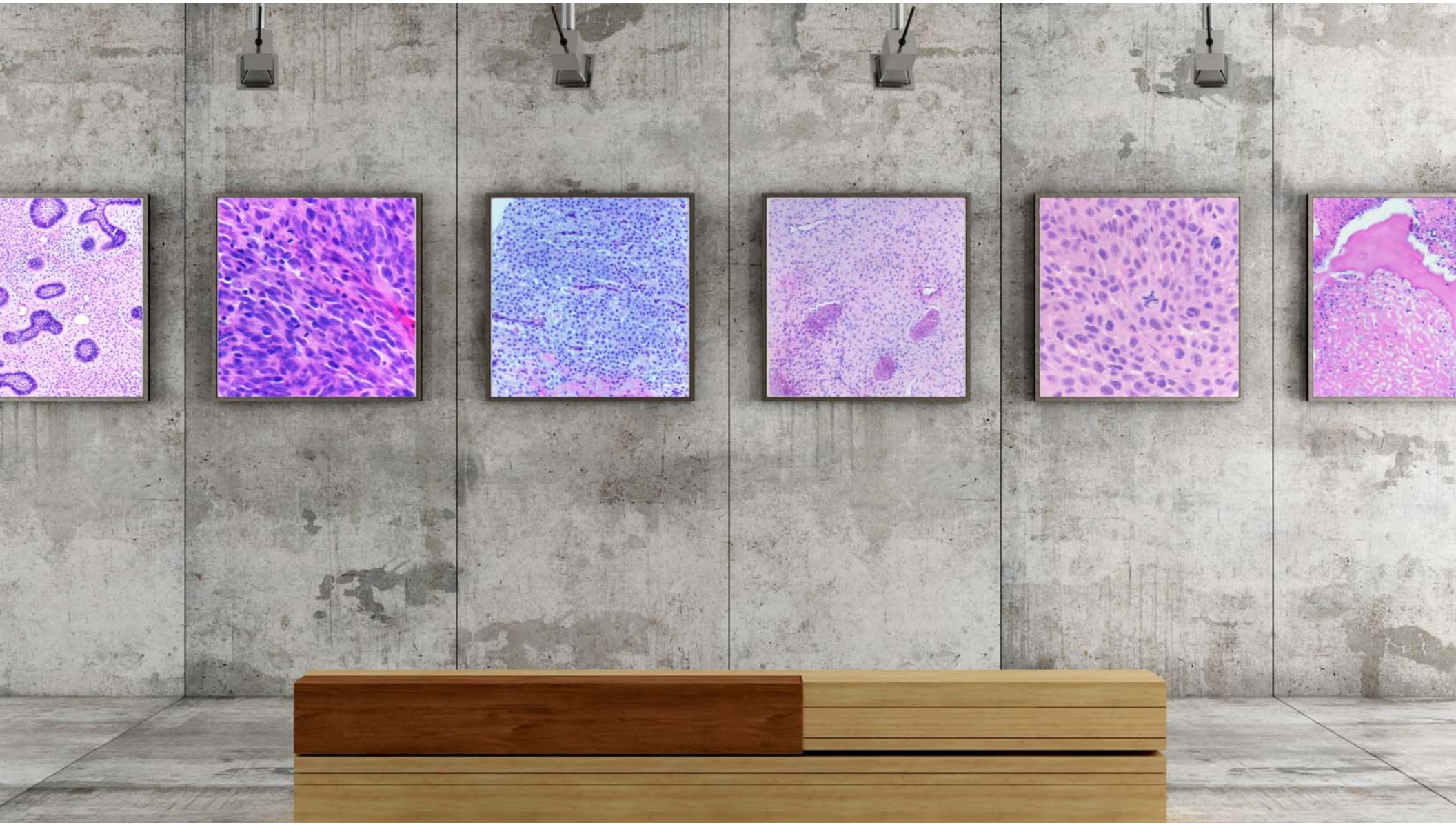

Resection
specimen


Resection
specimen

Osteoid osteoma of the mandible


cFOS


cFOS



daniel.baumhoer@usb.ch