



XXIV Congresso da
Sociedade Brasileira de
RADIOTERAPIA

17 A 20 DE AGOSTO | 2022 | FLORIANÓPOLIS/SC

RADIOTERAPIA PALIATIVA DE SARCOMA MIELÓIDE EM PULMÃO

RELATO DE CASO

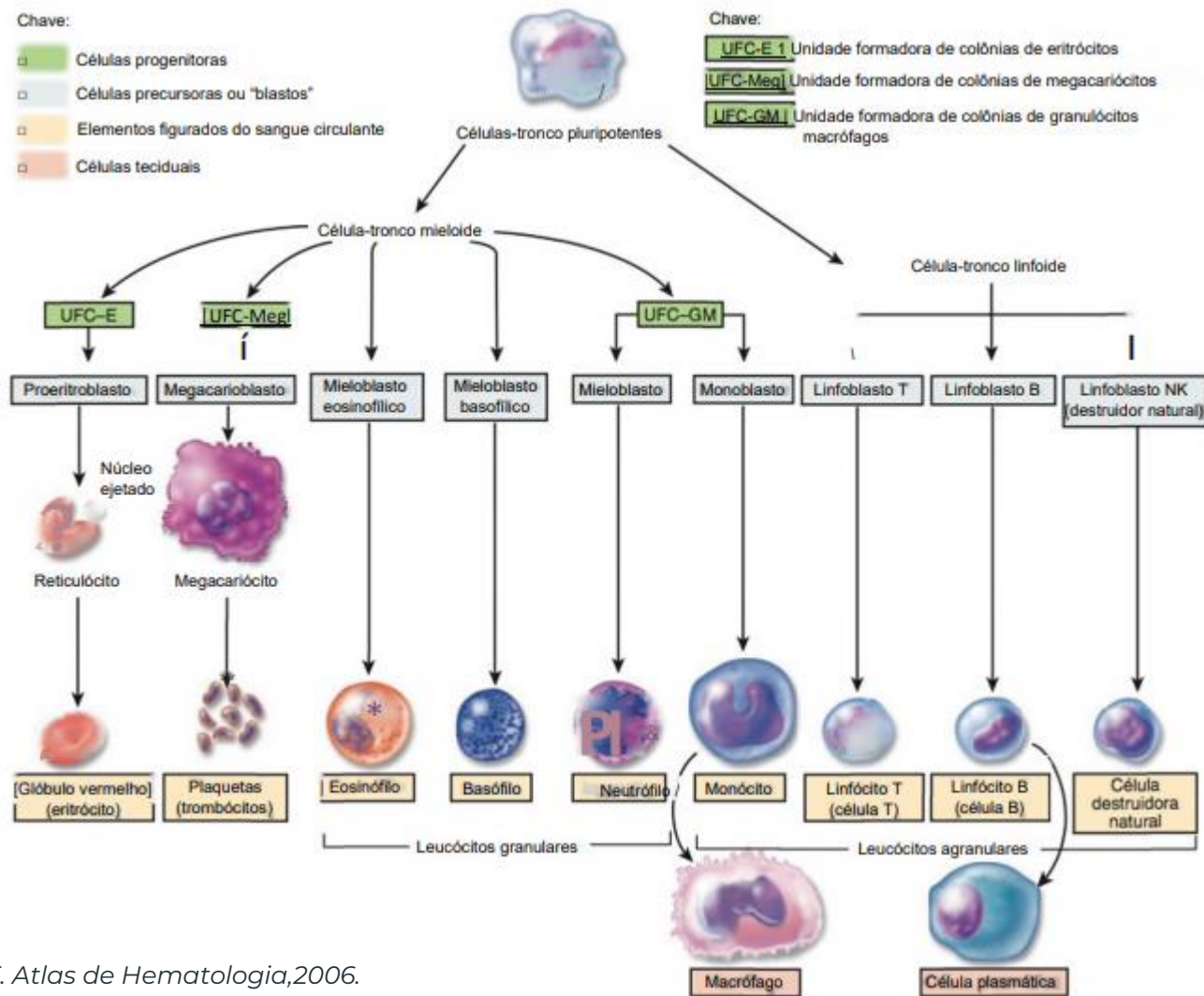
Jenifer Machado Ferraz
Técnica em Radioterapia - CRTR 09588T
COC Erechim Centro de Câncer

Chave:

- Células progenitoras
- Células precursoras ou "blastos"
- Elementos figurados do sangue circulante
- Células teciduais

Chave:

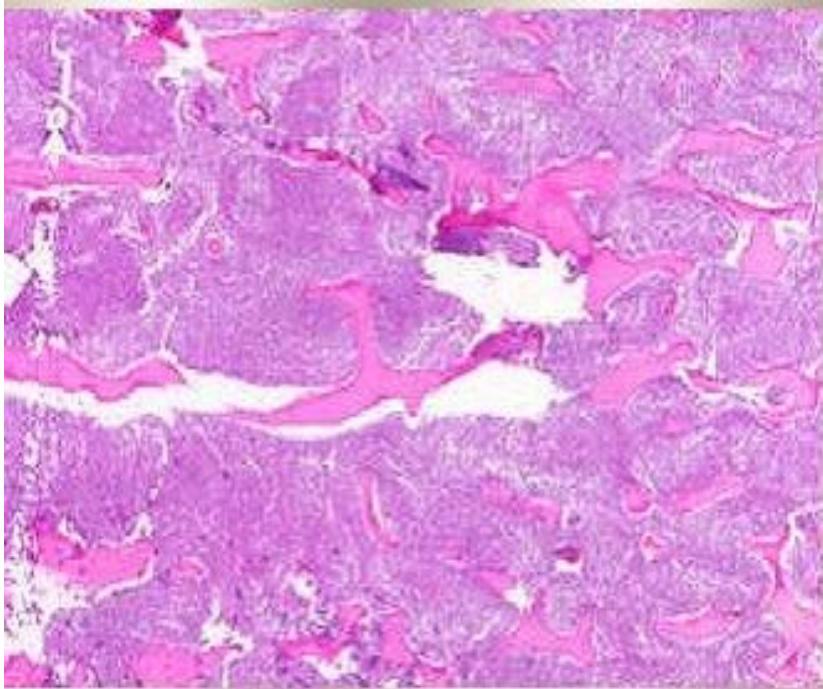
- UFC-E † Unidade formadora de colônias de eritrócitos
- UFC-Meg † Unidade formadora de colônias de megacariócitos
- UFC-GM † Unidade formadora de colônias de granulócitos macrófagos



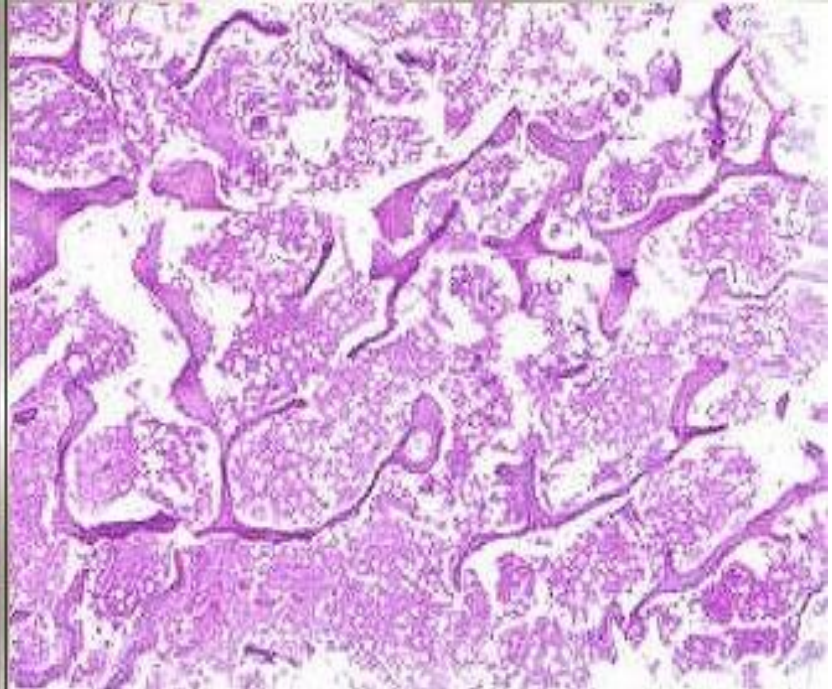
LEUCEMIA MIELÓIDE AGUDA (LMA)

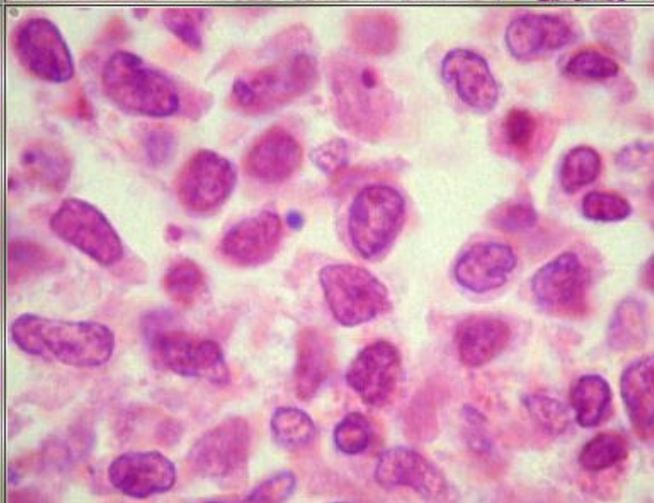
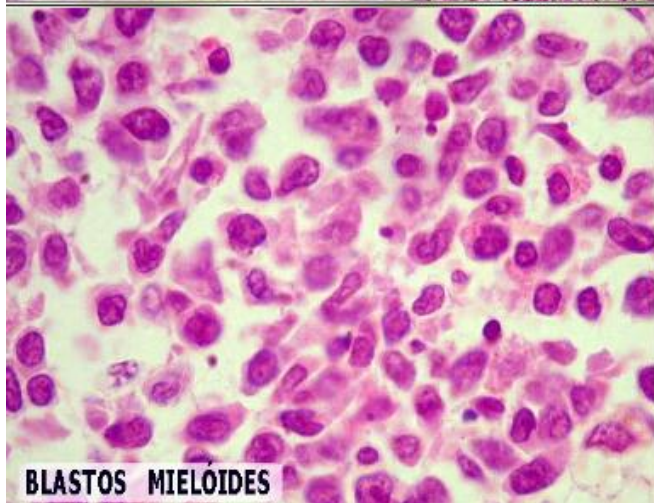
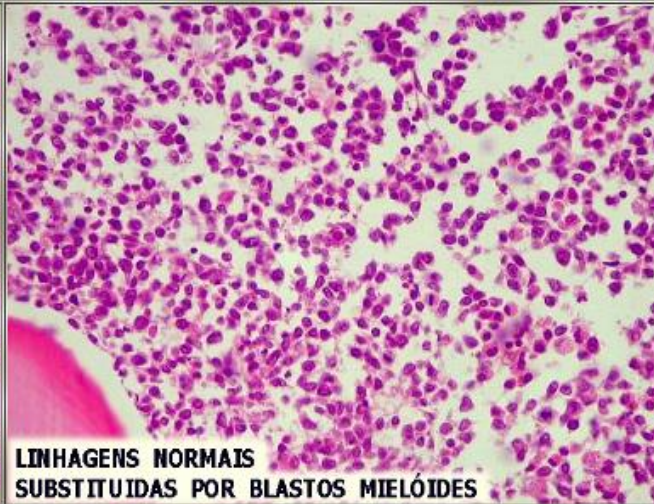
Grupo **heterogêneo** de doenças **clonais** caracterizados pela proliferação anormal de células hematopoiéticas **progenitoras**.

LEUCEMIA MIELÓIDE AGUDA



MEDULA ÓSSEA NORMAL







Prevalência

90% dos casos
ocorrem em adultos

Ranking Mundial

11º Incidência
10º Mortalidade

Fatores

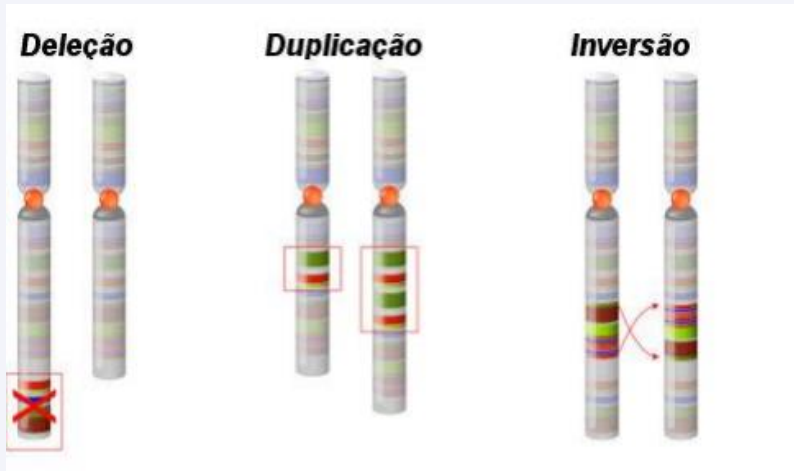
Ambientais, radiação
ionizante, benzeno,
alterações genéticas



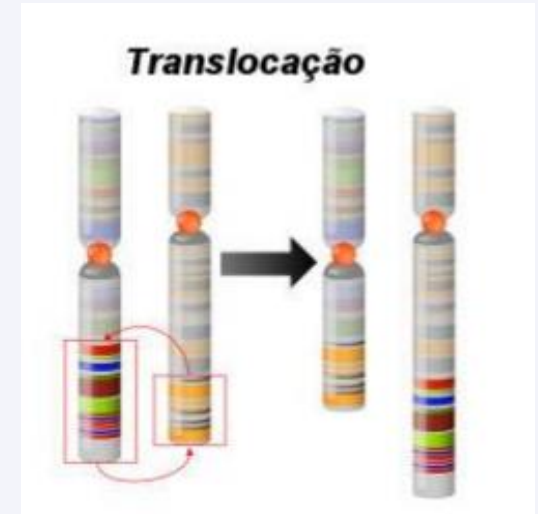
Alterações que afetam fatores de transcrição mielóide que controlam a diferenciação celular.

Mutações em genes que resultam na ativação anormal da função de proteínas.

Mutação cromossômica: translocação de genes altamente presente.



Diagnóstico





Falência da hematopoiese e/ou da infiltração de células leucêmicas em órgãos e tecidos.



Anemias, infecções , trombocitopenia.

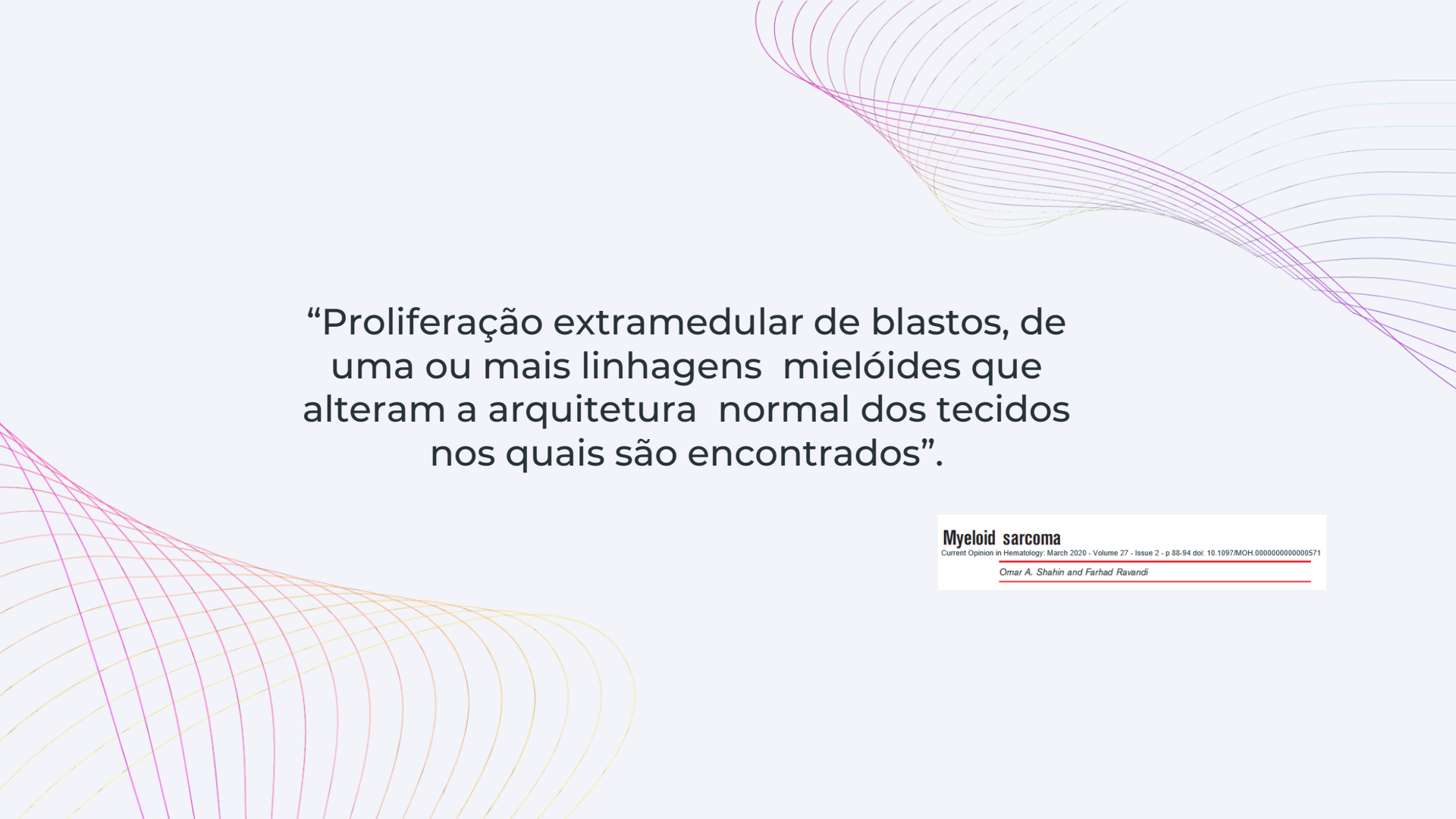


Presença de pelo menos 20% de blastos leucêmicos em aspirado de medula óssea ou em sangue periférico.



SARCOMA MIELÓIDE

**Cloroma; Sarcoma Granulocítico;
Mieloblastoma.**

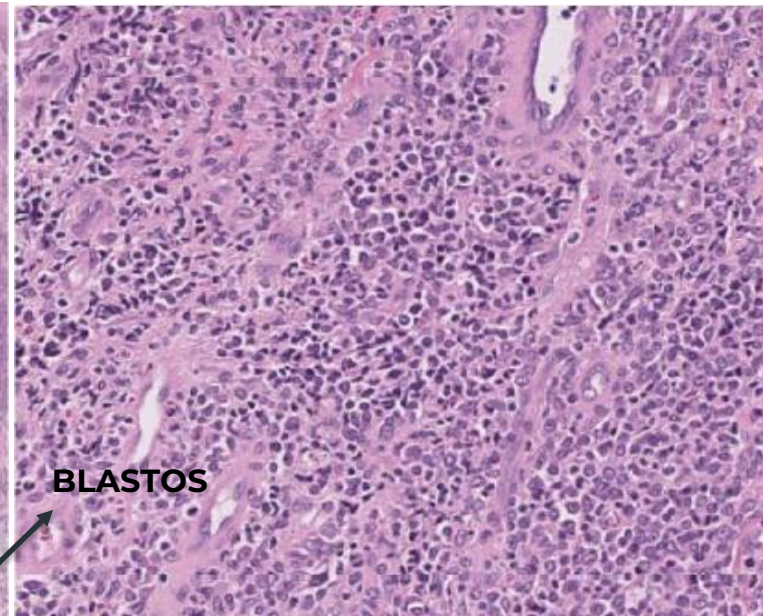
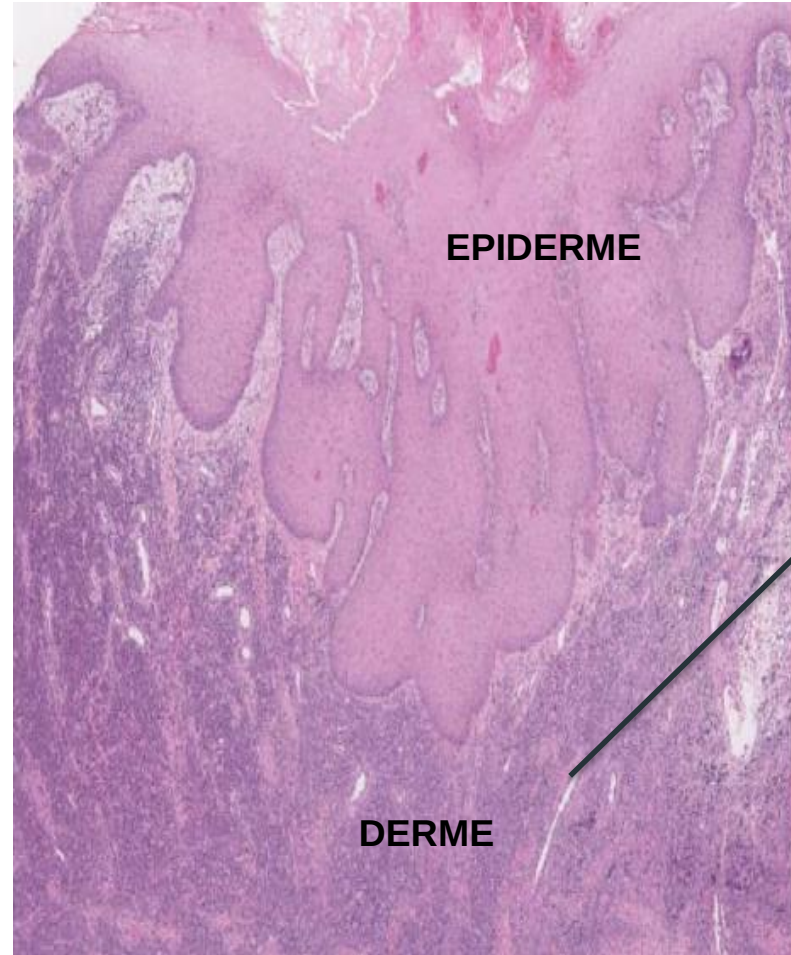


“Proliferação extramedular de blastos, de uma ou mais linhagens mielóides que alteram a arquitetura normal dos tecidos nos quais são encontrados”.

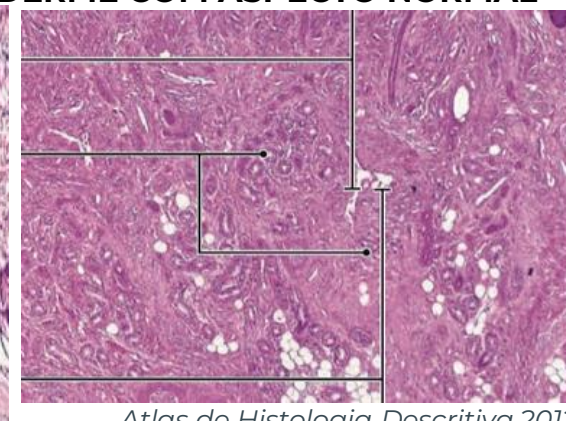
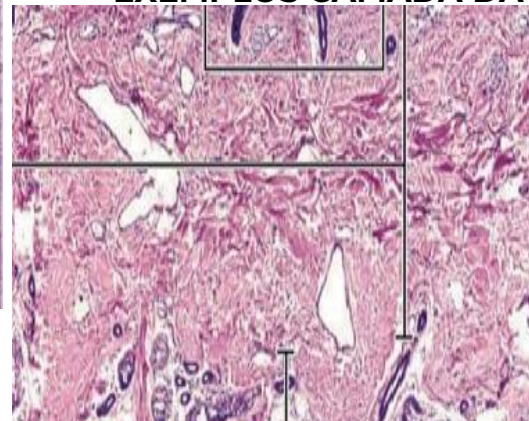
Myeloid sarcoma

Current Opinion in Hematology, March 2020 - Volume 27 - Issue 2 - p 88-94 doi: 10.1097/MOH.0000000000000571

Omar A. Shahin and Farhad Ravandi



EXEMPLOS CAMADA DA DERME COM ASPECTO NORMAL



**INFILTRADO ATÍPICO EM DERME- CÉLULAS
IMATURAS- SARCOMA MIELÓIDE**

Os sítios extramedulares ocorrem mais frequentemente em linfonodos, tecidos moles, osso, peritônio, trato gastrointestinal, mediastino e SNC.



Prévio a LMA (rara).



Manifestação de recaída em pacientes que se encontram em remissão de LMA.



Evolução para LMA em pacientes diagnosticados com síndrome mielodisplásica.

AJCP / SHIPAH® Women

Myeloid Sarcoma

Extramedullary Manifestation of Myeloid Disorders

Cristina Campidelli, MD, Claudio Agostinelli, MD, Richard Sittson, FRCPath, and Stefano A. Pileri, MD

Key Words: Myeloid sarcoma; Phenotype; Fluorescence in situ hybridization; FISH; Cytogenetics; Molecular biology
DOI: 10.1006/ajcp.12a11v02a215

Purpose of review

Myeloid sarcoma; also known as granulocytic sarcoma and chloroma, often occurs concomitantly with AML, and rarely without bone marrow involvement. In this article, we review the recent literature on myeloid sarcoma, focusing on treatment approach for this rare disease, and addressing the prognostic and therapeutic role of molecular and cytogenetic aberrations.

Recent findings

Molecular testing and cytogenetics are important in the diagnosis and prognostic significance of cytogenetic and molecular abnormalities, but testing for targetable mutations on myeloid sarcoma is not yet standard. Outcomes in myeloid sarcoma are poor. Almost all patients with myeloid sarcoma require systemic therapy. Postremission therapy is controversial and should be considered according to patient characteristics.

Summary

Further research is required to understand the role of molecular testing in clinical trials should be considered. The therapeutic approach in managing this rare disease is still unclear.

Keywords

chloroma, extramedullary leukemia, myeloid sarcoma

TREATMENT

There is no consensus on treatment of myeloid sarcoma because of the rarity of the disease and lack of randomized controlled studies. As virtually all patients with myeloid sarcoma eventually develop AML; treatment with AML protocols is the most reasonable approach. Management of myeloid sarcoma is dependent upon a number of factors; the site of the tumor (skin, CNS, others) and the timing of myeloid sarcoma (upfront, relapse after chemotherapy, relapse after hematopoietic stem cell transplantation). Other important factors are patient-related like age and performance status [3,14,29,44]. Depending on the aforementioned factors, variable modalities of treatment can be utilized, including chemotherapy, radiotherapy, hematopoietic stem cell transplantation, targeted therapies, and immunotherapies.

is uncertain in isolated myeloid sarcoma.

Radiotherapy in myeloid sarcoma was evaluated in limited trials, and although one trial suggested a potential survival benefit for the addition of radiotherapy to chemotherapy [40], a large retrospective analysis of 71 patients (from 7 large case series), showed no added benefit of combining radiotherapy and chemotherapy (19 vs. 24 months, $P = 0.41$) [49]. The use of radiation therapy in isolated myeloid sarcoma is recommended in cases of inadequate response to chemotherapy, and should be considered as consolidation if toxicities of radiotherapy are limited [50[¶]]. It should be noted that the use of radiotherapy in setting of myeloid sarcoma does not preclude total body irradiation if transplant is being considered [44]. Palliative doses of radiotherapy can be also provided for rapid symptomatic relief especially in the setting of vital organ function compromise (e.g. spinal cord compression, superior vena cava obstruction, etc.).

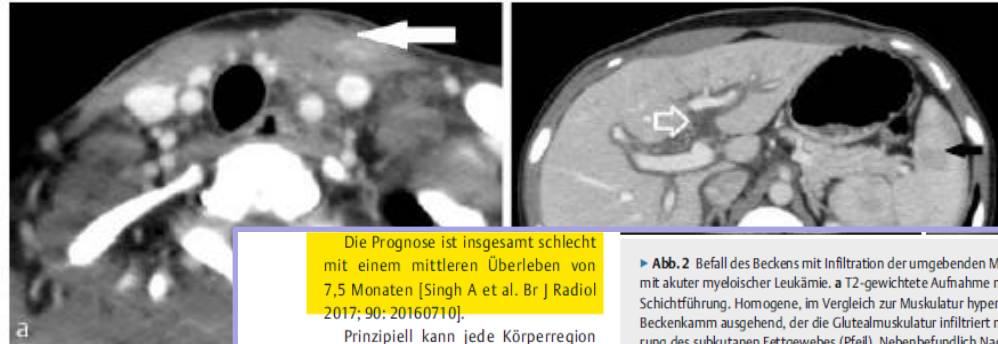
Rofo 2021; 193(01): 7-10 DOI: 10.1055/a-1150-8131

Myeloides Sarkom

Myeloid sarcoma

Einleitung

Das myeloide Sarkom, Chlorom oder granulozytische Sarkom ist ein solider extra-medullärer Tumor, bestehend aus Vorstufen myeloischer Blutzellen. Das Auftreten ist mit hämatologischen Erkrankungen aus der myeloischen Reihe der Leukozyten assoziiert, am häufigsten mit der akuten myeloischen Leukämie (AML), nachrangig mit der chronischen myeloischen Leukämie, dem myelodysplastischen Syndrom und myeloproliferativen Syndromen. Es kann jedoch auch de novo entstehen oder einer Leukämie vorausgehen. Die Inzidenz des myeloiden Sarkoms reicht bei der AML von 2,5–30 %, wohingegen für die seltene-



► **Abb. 1** 26-jährige Patientin mit akuter myeloischer Leukämie. **a** T2-gewichtete Aufnahme mit Fettsättigung in axialer Schichtführung. Homogene, im Vergleich zur Muskulatur hyperintense Läsion vom linken Beckenkamm ausgehend, der die Glutealmuskulatur infiltriert mit angrenzender Ödematisierung des subkutanen Fettgewebes (Pfeil). Nebenbefundlich Nachweis von freier Flüssigkeit im kleinen Becken. **b** T1-gewichtete Aufnahme nach Kontrastmittelgabe mit Fettsättigung in axialer Schichtführung. Die Läsion zeigt eine moderate Kontrastmittelanreicherung mit peripherer Betonung.

Die Prognose ist insgesamt schlecht mit einem mittleren Überleben von 7,5 Monaten [Singh A et al. Br J Radiol 2017; 90: 20160710].

Prinzipiell kann jede Körperregion betroffen sein, am häufigsten zeigt sich jedoch der Befall der Weichteile (zu etwa 70 %), der Knochen und der Lymphknoten [Claerhout H et al. Eur J Haematol 2018; 100:603–612; Meyer HJ et al. Radiol Oncol 2019; 53: 213–218; Ooi GC et al. AJR Am J Roentgenol 2001; 176: 1427–1431]. Es scheint keine Unterschiede der Lokalisationen von de novo und sekundären myeloiden Sarkomen zu geben [Claerhout H et al. Eur J Haematol 2018; 100: 603–612].

In etwa 50 % der Fälle sind die Läsionen symptomlos, in den übrigen Fällen sind die Symptome abhängig von der jeweiligen betroffenen Körperregion [Singh A et al. Br J Radiol 2017; 90: 20160710].

► **Abb. 2** Befall des Beckens mit Infiltration der umgebenden Muskulatur bei einem Patienten mit akuter myeloischer Leukämie. **a** T2-gewichtete Aufnahme mit Fettsättigung in axialer Schichtführung. Homogene, im Vergleich zur Muskulatur hyperintense Läsion vom linken Beckenkamm ausgehend, der die Glutealmuskulatur infiltriert mit angrenzender Ödematisierung des subkutanen Fettgewebes (Pfeil). Nebenbefundlich Nachweis von freier Flüssigkeit im kleinen Becken. **b** T1-gewichtete Aufnahme nach Kontrastmittelgabe mit Fettsättigung in axialer Schichtführung. Die Läsion zeigt eine moderate Kontrastmittelanreicherung mit peripherer Betonung.

berichteten Inzidenz von bis zu 70 % der Fälle. Diese treten häufig multipel auf. In

► **Abb. 1** stellen wir einen Patienten mit multiplen, muskulär lokalisierten Läsionen vor. Der muskuläre Befall kann hierbei primär oder sekundär aus einem knöchernen Befallsmuster hervorgehen. Diese sind meist homogen und kontrastmittelaufnehmend. Relativ typisch für das myeloide Sarkom ist der Befall des Beckens. Der von uns gezeigte Fall zeigt einen sekundären Befall der Glutealmuskulatur (► **Abb. 2**).

tisch-hypersklerotisches Muster gesehen werden.

Intrakraniell manifestiert sich das myeloide Sarkom am häufigsten in extraaxialer Lokalisation. Hierbei können epidurale und subdurale, relativ homogene Läsionen gefunden werden. Wir stellen einen Fall vor, in dem die präpontine Zisterne durch eine weichteildichte Formation befallen ist (► **Abb. 4**). Auffällig ist vor allem die starke Diffusions einschränkung des Befundes als Hinweis für eine hohe Zell-

RADIOTERAPIA



ORIGINAL ARTICLE

Radiotherapy for extramedullary leukaemic manifestation (Chloroma)

Michael Oertel¹  · Khaled Elsayad¹ · Uwe Haverkamp¹ · Matthias Stelljes² · Hans Theodor Eich¹

Received: 23 May 2017 / Accepted: 26 October 2017
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Abstract

Purpose Extramedullary leukaemic disease (ononym chloroma) is a rare solid manifestation leukaemia for which the value of radiotherapy as a treatment strategy remains controversial. The study is to analyse the effectiveness of various RT for EMD in the modern treatment era.

Materials and methods Between January 2008 and 2016, 20 patients with total of 45 lesions underwent EMD at our institution.

Results With a median radiation dose of 26 Gy (range

Studies examining the prognostic value of different treatment modalities are sparse as patient numbers are low and nearly all analyses are retrospective. Intensive chemotherapy is usually used in patients with EMD resulting in a regression of lesions in the majority of patients [2, 6]. Furthermore, allogeneic hematopoietic stem cell transplantation (HSCT) may represent a feasible treatment with long-lasting effect, especially in unfavourable prognostic subgroups of AML patients [14]. The European LeukemiaNet (ELN) recommendations on diagnosis and management of AML were actually revised to reflect recent changes in the understanding of the biology and prognosis of genetically defined subgroups [15].

Nevertheless radiotherapy (RT) has proven to provide excellent local control resulting in good symptomatic relief [6, 11, 12]. Recently, low-dose RT regimens for various haematological conditions showed efficient short-term relief of symptoms and minimal toxicity profiles [6, 16, 17].

However, in lack of randomized prospective trials, treatment for chloroma in general remains elusive. Therefore, the aim of our study was to evaluate the impact of various RT doses on chloroma in the modern era of molecular cytogenetics and combined modality therapy.

was calculated from the first day of radiation. Progression-free survival (PFS) was calculated from the initiation of RT therapy until the time of documented relapse or death, while duration of local control (DOLC) was calculated until the time of documented local relapse after RT or death. Differences were considered statistically significant at a P -value < 0.05 . Independent variables were first analysed with univariate analysis. Variables shown by univariate analysis to be associated with local control or survival ($P < 0.1$) were entered into a Cox proportional hazards regression model for multivariate analysis.

Definition of response

EMD response was assessed during RT aiming to conduct adaptive planning of large lesions, and then at a 3-month follow-up appointment. Complete response (CR) was defined as complete clinical regression of all irradiated lesions, while partial response (PR) represented any response less than complete that showed $> 50\%$ radiological and/or clinical improvement. Local progression was defined as $> 25\%$ clinical progress of the lesions. Further investigation using positron emission tomography-computed tomogra-



RADIOSENSIBILIDADE DE ALGUNS TECIDOS E CÉLULAS

MUITO SENSÍVEIS	MEDIANAMENTE SENSÍVEIS	MENOS SENSÍVEIS
1.0 – TECIDO HEMATOPOIÉTICO	3.0 – CÉLULAS ENDOTELIAIS	6.0 – CÉLULAS ÓSSEAS
1.1 –Linfócitos 1.2 – Eritroblastos 1.3 - Mieloblastos	3.1 Vasos sanguíneos	6.1-Osteoblastos 6.2-Osteoclastos 6.3-Osteócitos
2.0 – CÉLULAS EPITELIAIS	4.0 – TECIDO CONECTIVO	7.0 – CÉLULAS NERVOSAS
2.1 – Testículos 2.2 – Ovários 2.3 - Pele	4.1 – fibroblastos 4.2 – fibrócitos	7.1- Células da glia 7.2 células de Schwann
	5.0 – CÉLULAS TUBULARES DOS RINS	8.0 – CÉLULAS MUSCULARES

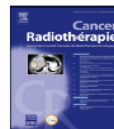


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Revue générale

Radiothérapie des chloromes ou sarcomes granulocytiques :
revue de la littérature

Radiotherapy of chloroma or granulocytic sarcoma: A literature review

S. Yossi^{a,*}, S. de Talhouet^a, S. Ducastelle-Leprêtre^b, A. Hassouni^{a,c}, G. Pigné^a, I. Selmaji^{a,d},
H. Samlali^{a,c}, M. Ginoux^a, I. Caraivan^a, A. d'Hombres^a

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Grupo de 33 pacientes

Grupo 10 Gy – 18%

Grupo 10 a 19,9 Gy – 43%

Grupo 20 a 29,9 – 86 %

Grupo 30 Gy – 89%

Resultado: dose biologicamente efetiva superior a 20Gy
Sugerindo- se protocolo de 24 Gy em 12 frações

Treatment of Extramedullary Myeloid Sarcoma With Radiotherapy

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Corresponding author: Suzanne R. Graham, rgraham37@qub.ac.uk

However, even low-dose radiotherapy can achieve excellent local response and control, which can be particularly useful when the myeloid sarcoma is causing local symptoms or in palliation, such as in the case discussed. Myeloid sarcomas are radiosensitive, and complete response rate was found to be 89% where over 30 Gy was used, dropping to 43% when under 20 Gy was used [11]. Therefore, it is recommended to use at least 20 Gy, though some literature suggests that 24 Gy in 12 fractions may be optimal for local control [12].

Conclusions

This case of a gentleman presenting with an orbital mass, which led to a diagnosis of myeloid sarcoma, highlights the difficulty in diagnosing this rare pathology. Due to its rarity, it is often misdiagnosed, and research surrounding myeloid sarcoma remains limited. Diagnosis of this pathology in a timely manner is critical to aid prompt patient management and prognosis. It is also important to note that it is radiosensitive and low-dose radiation can achieve excellent local control and alleviation of symptoms.

Introduction

Myeloid sarcoma (also known as chloroma, granulocytic sarcoma, or myeloblastoma) is a rare extramedullary manifestation of acute myeloid leukaemia (AML) with an estimated incidence throughout the literature of under 1% [1]. This rare neoplastic condition, which consists of immature myeloid cells, most often occurs in areas such as bone and skin; however, almost any area of the body can be affected. It can sometimes be the first manifestation of AML in a patient, precede a diagnosis of AML, or even be the initial finding in a patient who has relapsed from previously treated AML [2,3].

s. In this paper, we report the case of
d to be a myeloid sarcoma. We also

ml), radiotherapy (rt), palliative



CASO CLÍNICO

- 
- Paciente feminino, 43 anos

LMA – M5 Cardio complexo- Alto Risco – janeiro 2020- em outro serviço

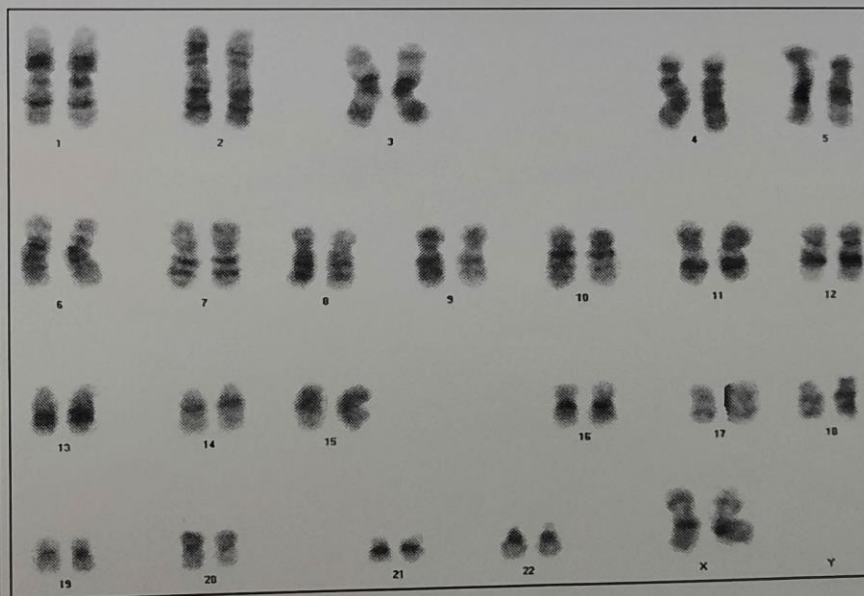
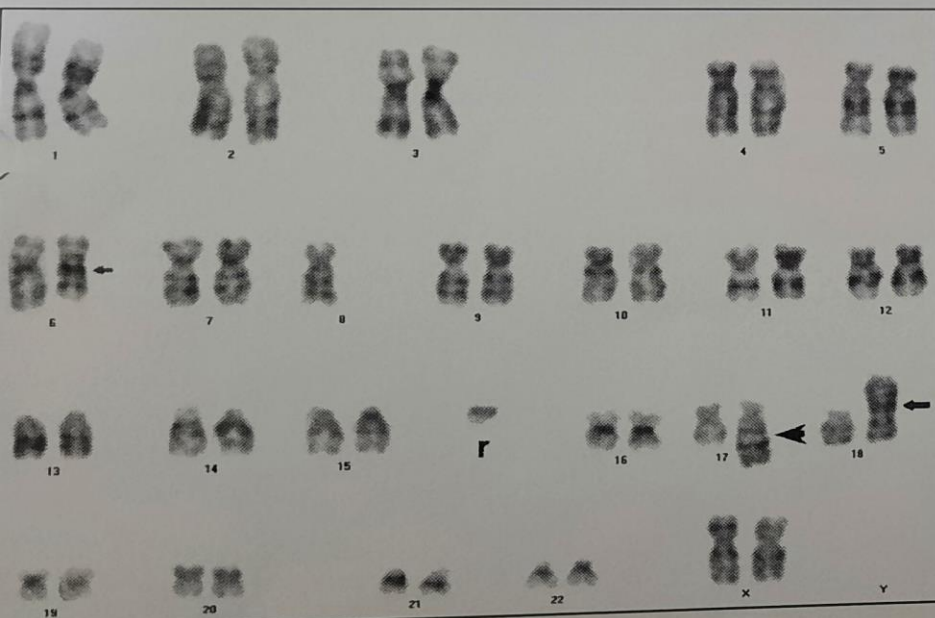


Resultado

46,XX,der(6)t(6;8)(q13;q13),-8,der(17)t(1;17)(q25;q25),der(18)t(6;18)(q13;p11.3),+r[19]/
46,XX[1]

Conclusões e comentários

Análise citogenética revelou conjunto cromossômico feminino anormal, correspondente a clone neoplásico que mostra anormalidades múltiplas, entre as quais se destaca a trissomia de 1q, secundária à formação do derivado (1;17). Estes achados são consistentes com o diagnóstico clínico de LMA. Informações adicionais sobre trissomia de 1q em neoplasias mieloides podem ser acessadas nos endereços eletrônicos que seguem: <http://atlasgeneticsoncology.org/Anomalies/Unb1qMyeloidMalignID1638.html>.



- Julho/2020- início do tratamento neste serviço- remissão após término do protocolo de QT 7+3 seguido de altas doses de citarabina e aguarda TMO alogênico

Recaída precoce- 79% blastos em MO setembro/2020- protocolo de resgate IDA-FLAG e nova - Remissão novembro/2020 – blastos 3%

TCTH alogênico janeiro/2021 com irmã haplo-
>>>> 50% de blastos em medulograma (abril)- Recaída

maio 2021- protocolo de resgate AZA+ Venetoclax - Remissão-
Medulograma 4% de blastos- junho 2021

Segue QT- medulograma 2% blastos- outubro de 2021

- Novembro 2021 paciente apresenta dor lombossaca, perda da força MIE, constipação, bexiga neurogênica, dor supra escapular direita com redução da sensibilidade da mão ipsilateral.

19/11/21 Realizado exames de imagem – extensas lesões em cone medular, pleura, região esternal e mucosa retal.

MO sem evidência de doença

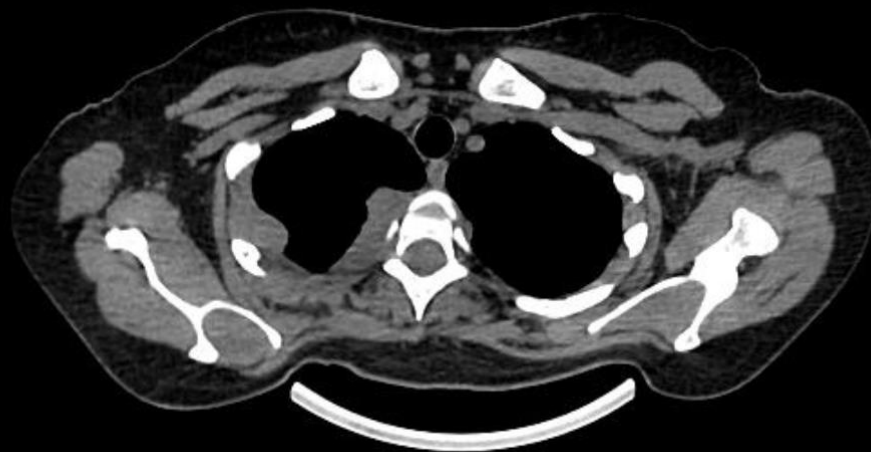
Biópsia em lesões- **Sarcoma mielóide**

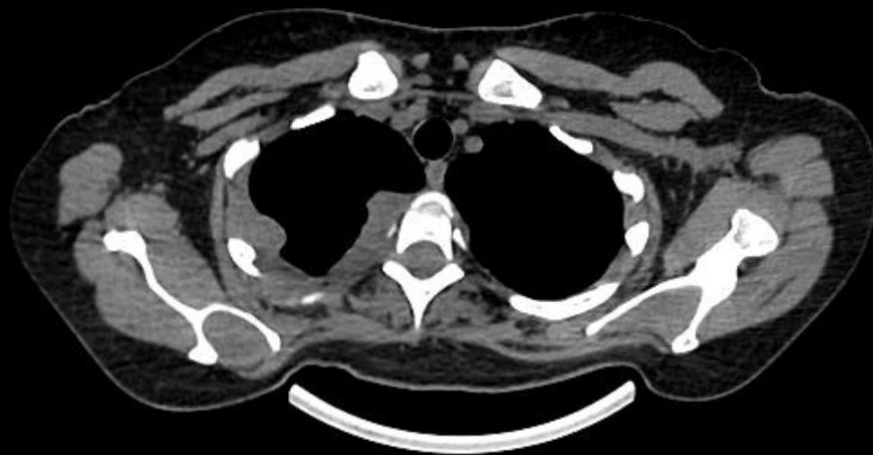
Paciente encaminhada para radioterapia











19/11/2021 - 16:43

NIVEL: 80

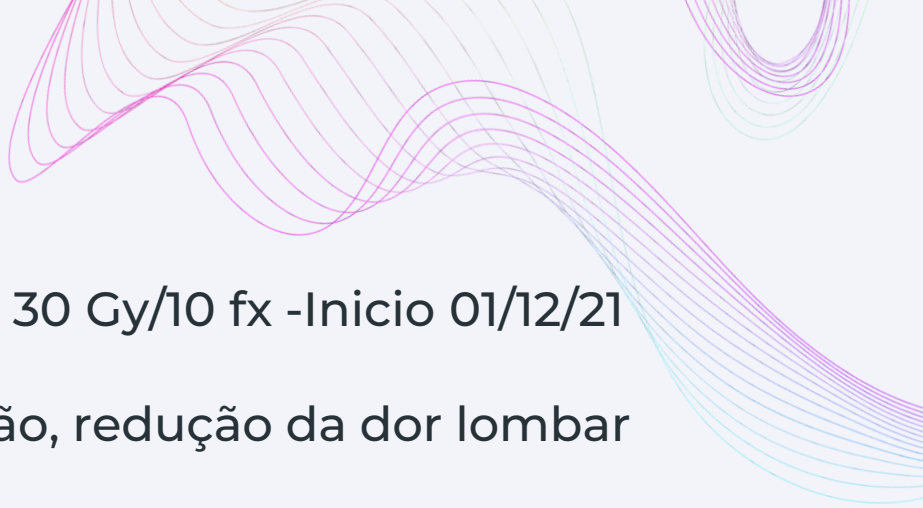


SERIE

FACIO

TORAX

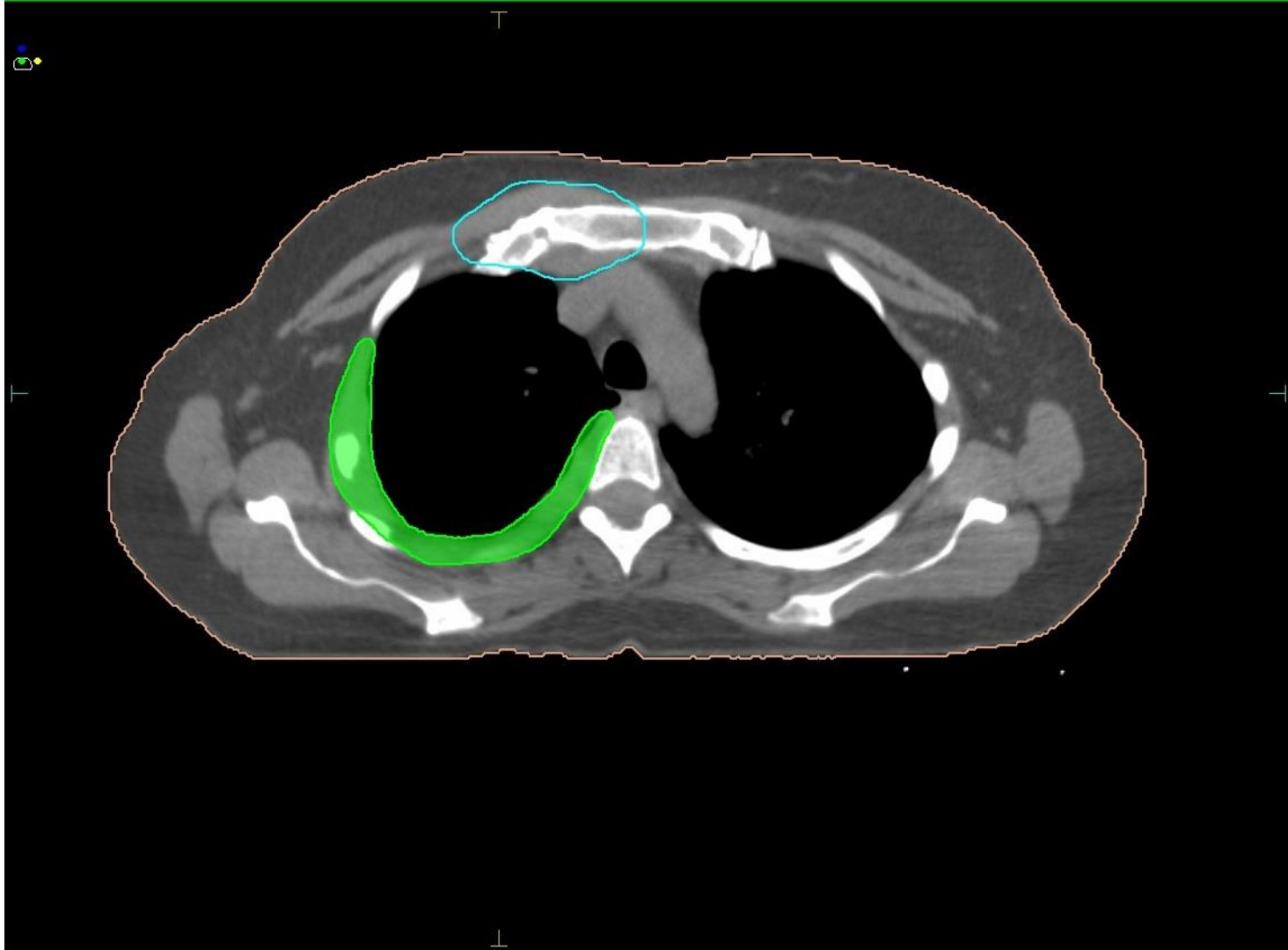


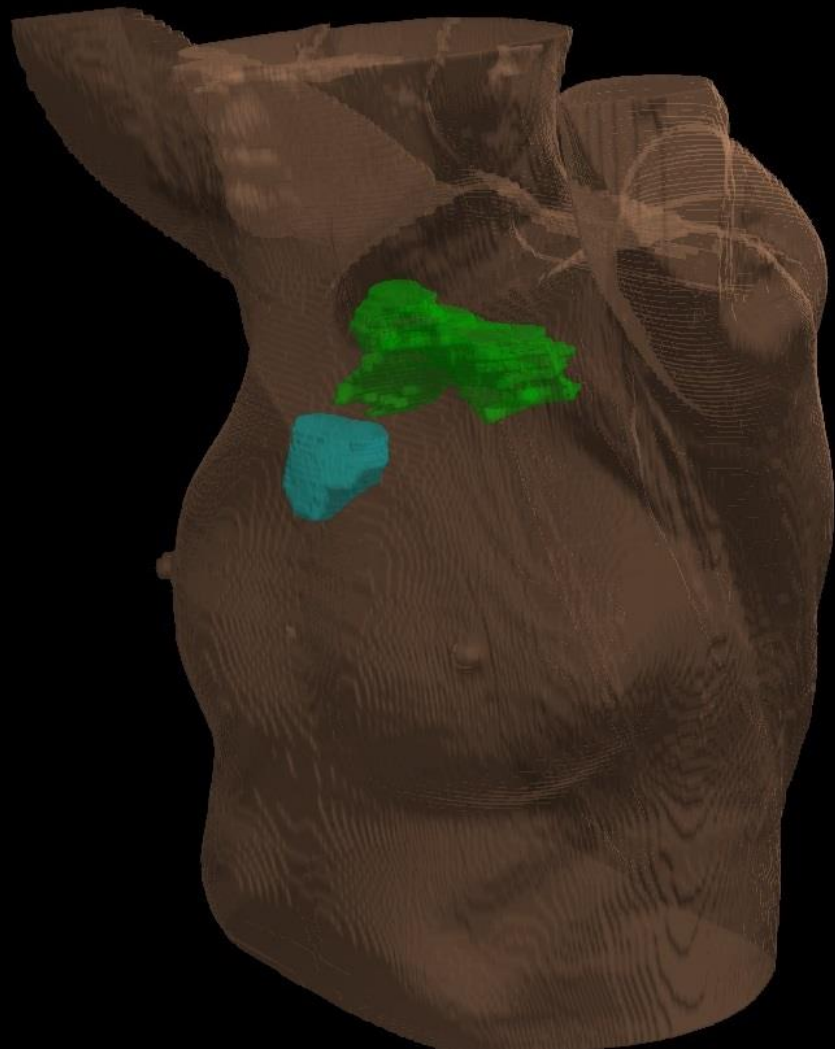


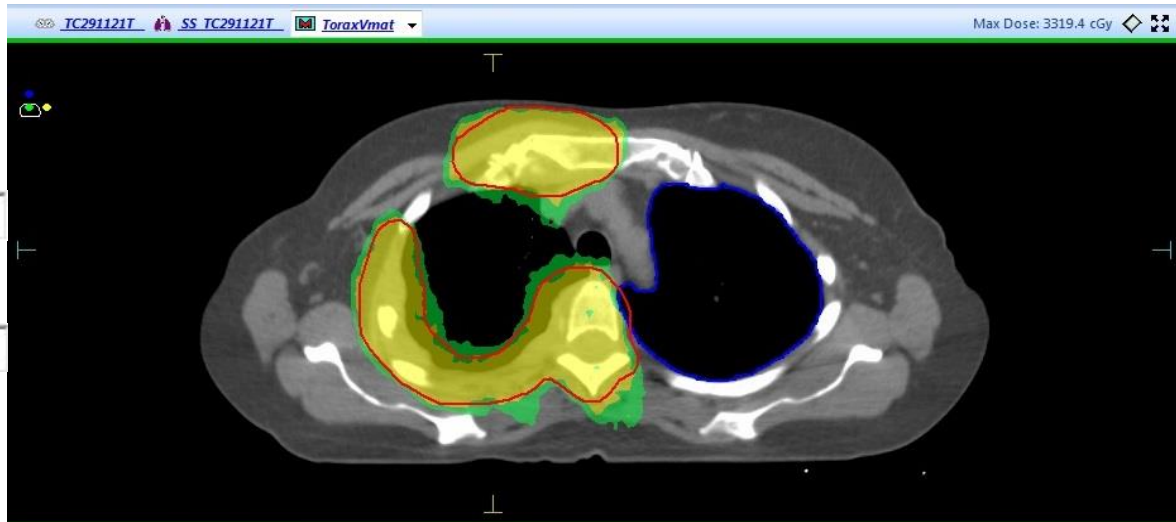
Programado RT em coluna lombar 30 Gy/10 fx -Início 01/12/21

14/12/2021- melhora na deambulação, redução da dor lombar

- 06/12/2021 Início da RT em tórax, pulmão direito, controle dos sintomas, 30 Gy/ 10 fx, IMRT
-

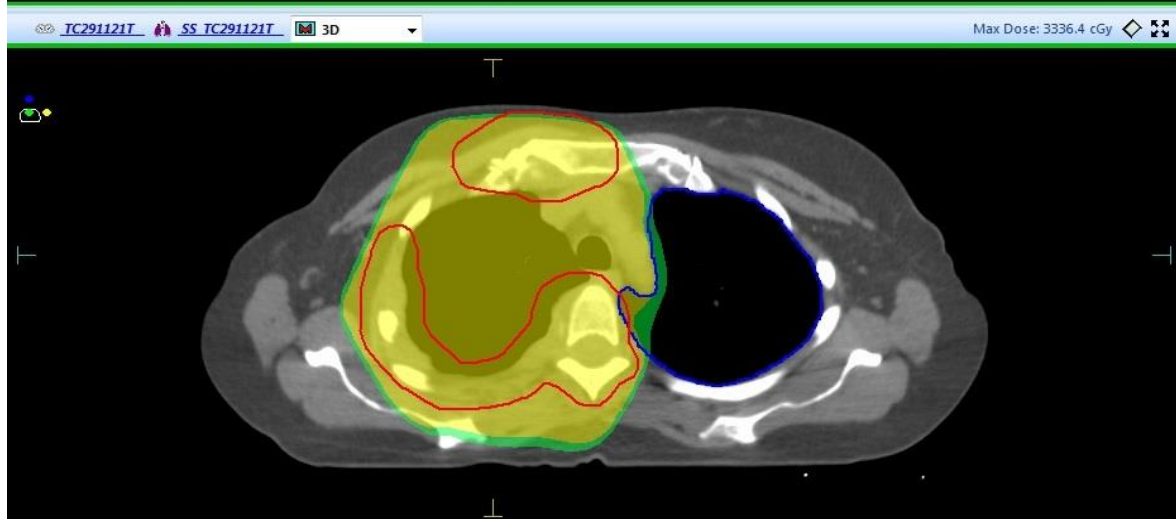






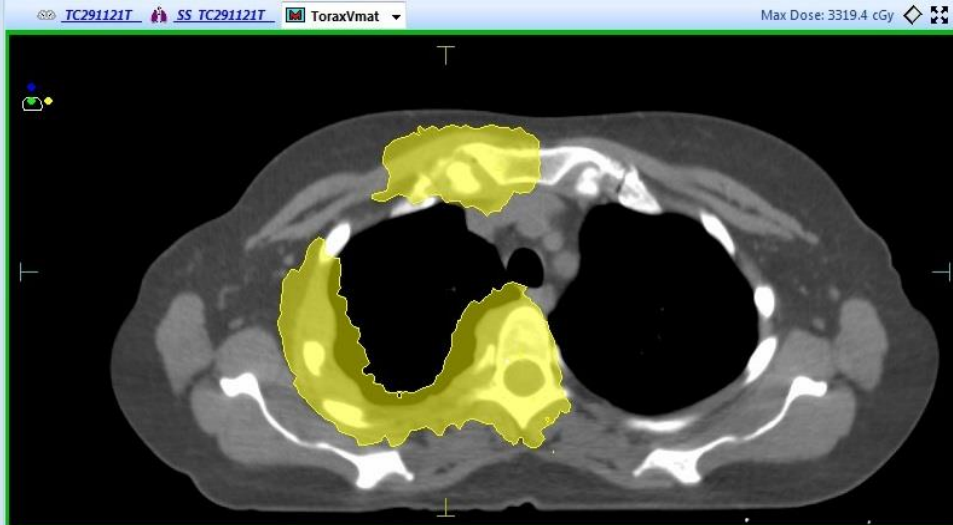
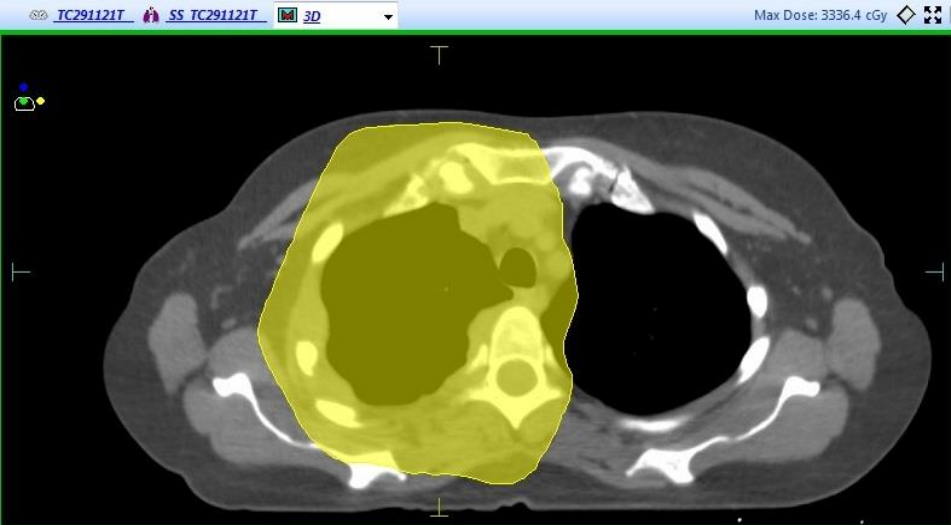
Dose de prescrição

Toxicidade



Dose baixa





Statistics | Display

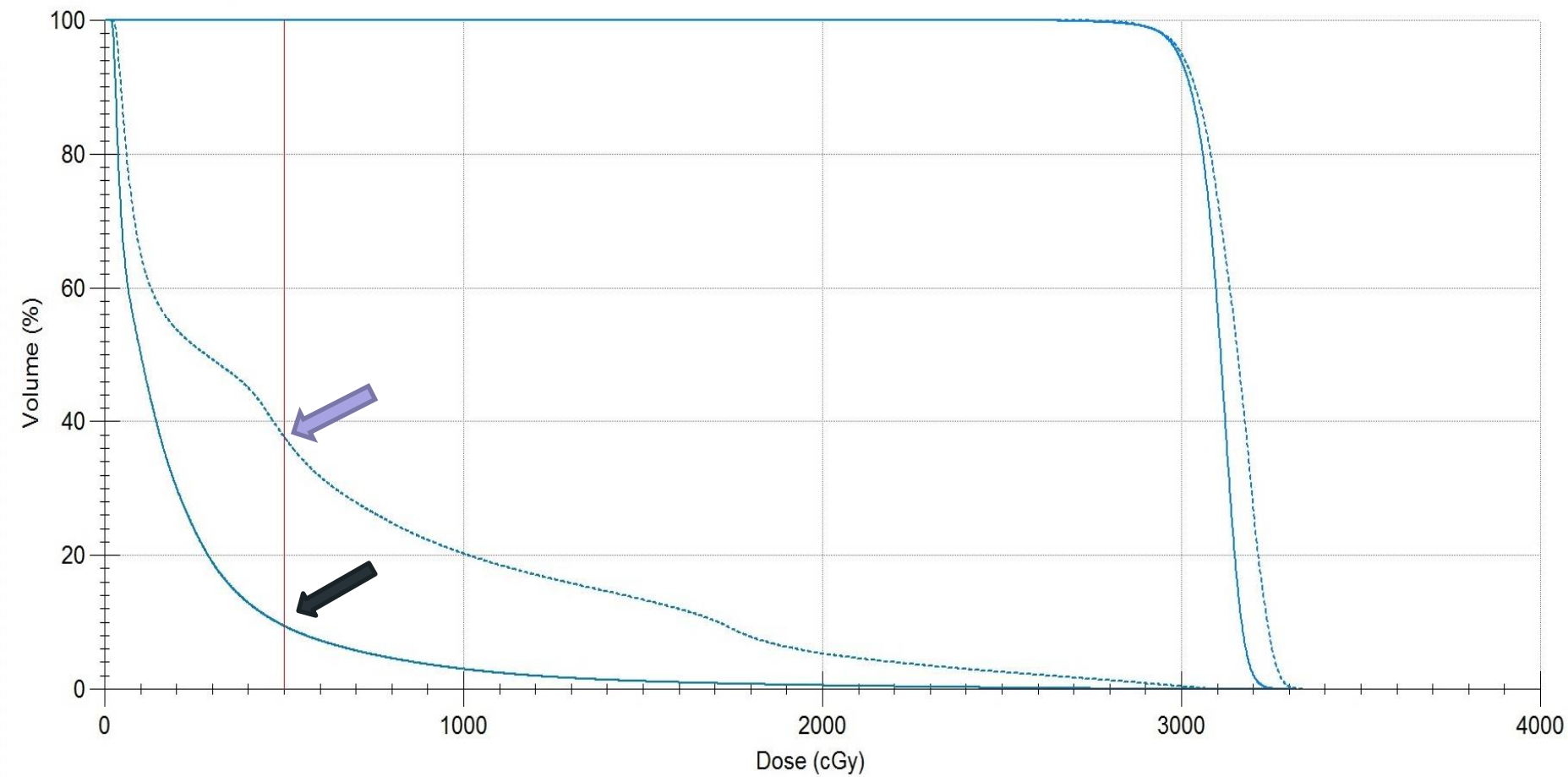
Structure	Plan	Min. Dose (cGy)	Max. Dose (cGy)	Mean Dose (cGy)	Hot Ref. (cGy)	Volume > (cm ³)	Volume > (%)
Pulmao D - PTV Total	3D	38.1	3250.7	845.2	3000.0	105.572	8.37
Pulmao D - PTV Total	ToraxVmat	46.5	3034.6	706.8	3000.0	0.015	0.00

Print

OK

ToraxVmat
(500.0, 9.41)

3D



Isodoses

100.00 % = 3000.0 cGy ☒ Relative Mode

Custom Save As

2D 3D

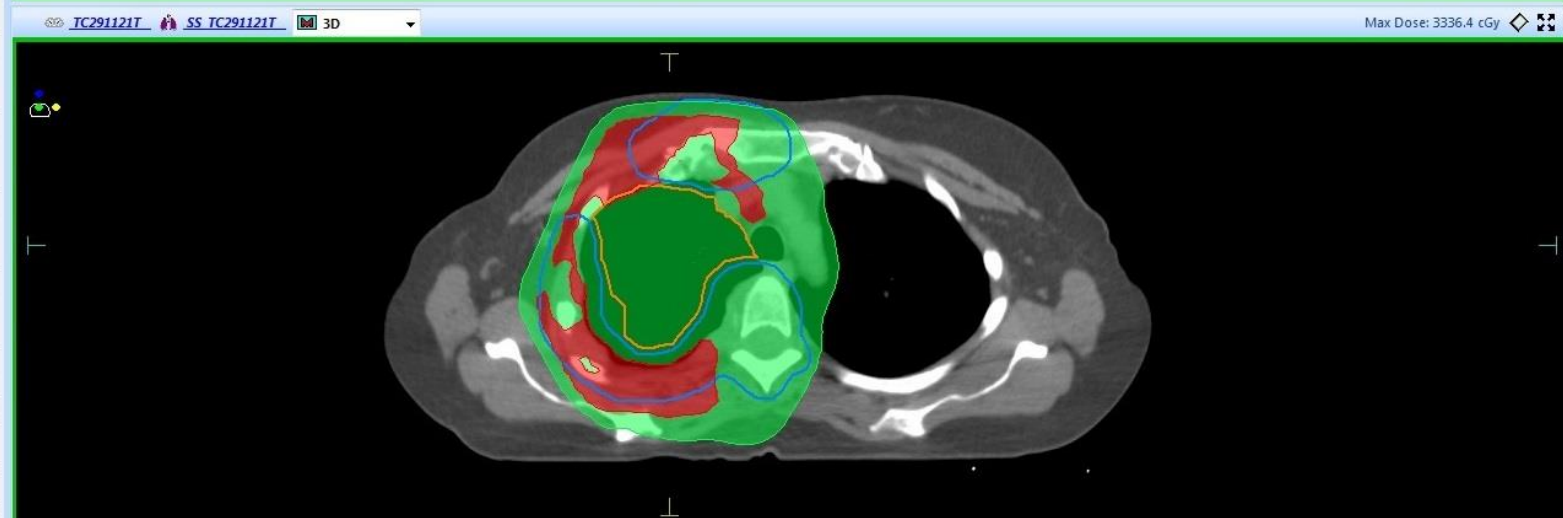
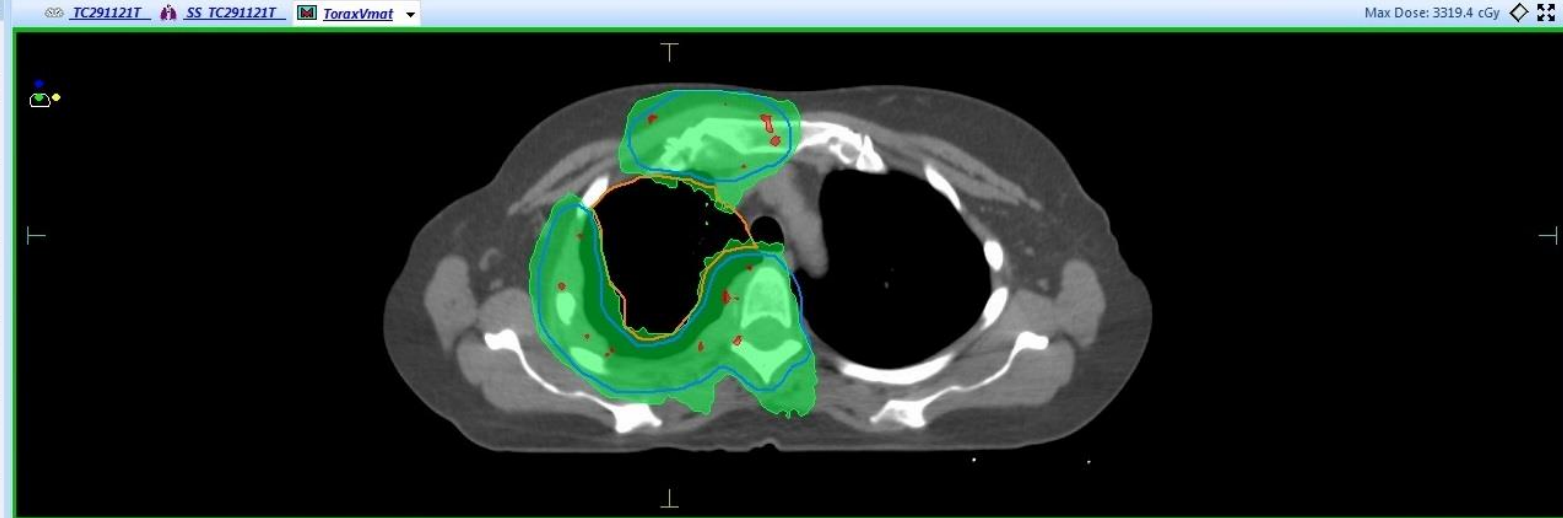
	107.00	W	W
	105.00	Off	W
	100.00	Off	Off
	95.00	Off	Off
	90.00	Off	Off
	80.00	Off	Off
	64.29	Off	Off
	50.00	Off	Off
	42.86	Off	Off
	28.57	Off	Off

All 2D Off All 3D Off

Thickness % 5 ☐ Isolines

Cutoff % 0

IsoFill



100.00 % = 3000.0 cGy ☒ Relative Mode

Custom Save As

2D 3D

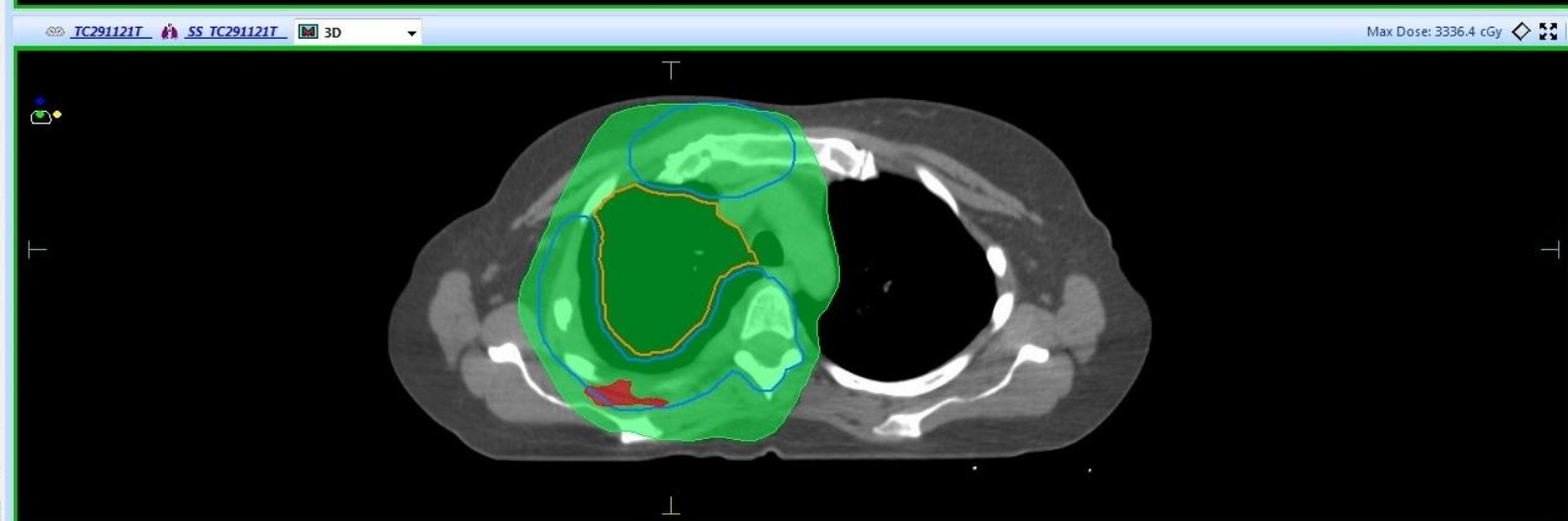
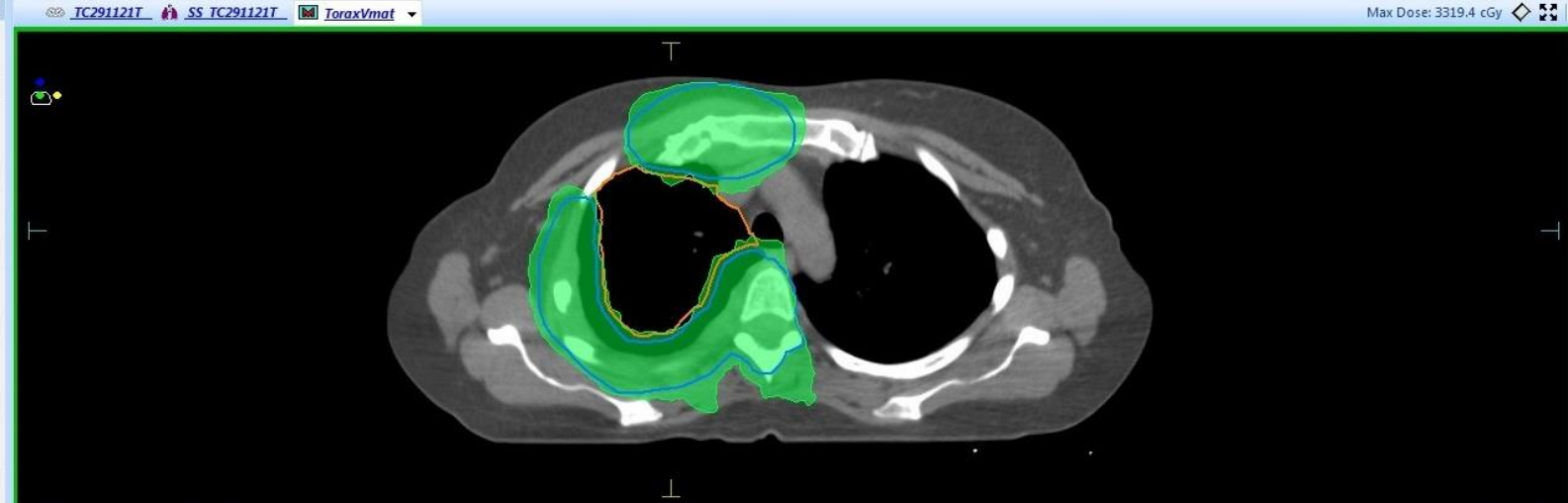
	110.00	W
	105.00	Off W
	100.00	Off Off
	95.00	Off
	90.00	Off Off
	80.00	Off Off
	64.29	Off Off
	50.00	Off Off
	42.86	Off Off
	28.57	Off Off

All 2D Off All 3D Off

Thickness % 5

Cutoff % 0 ☒ Isolines

IsoFill



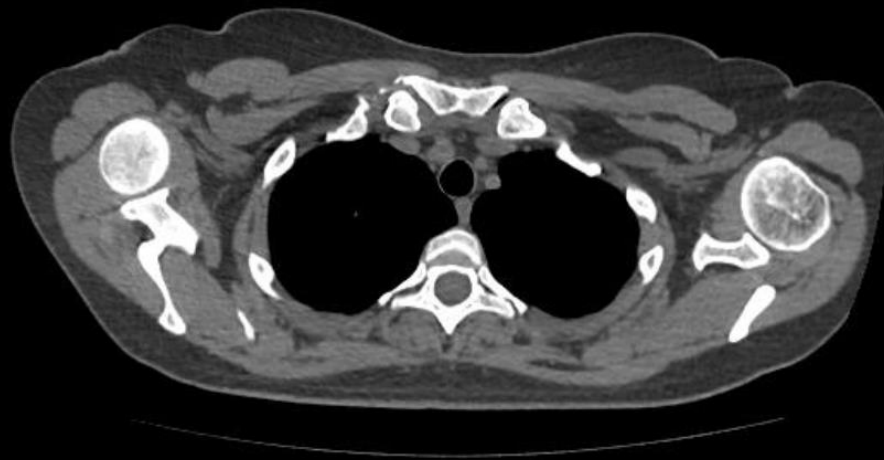
● 17/12/21- Completa RT em Tórax

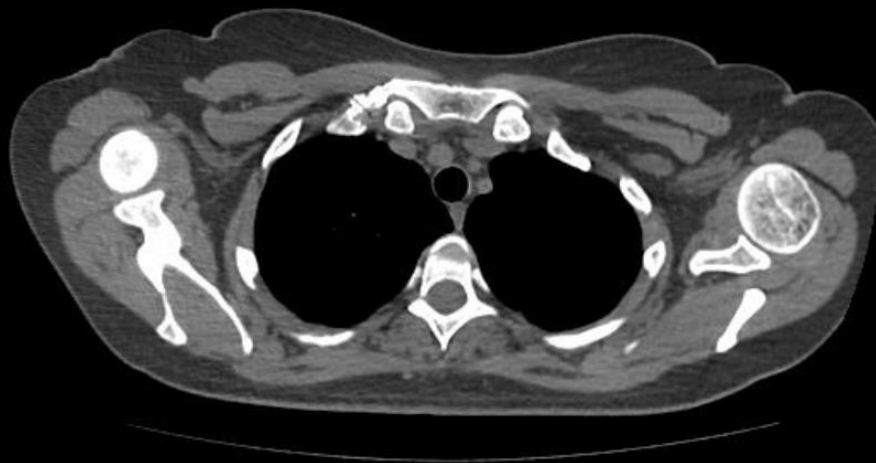
Melhora importante na força e redução da dor no
MSD

Odinofagia leve, mucosite esofágica

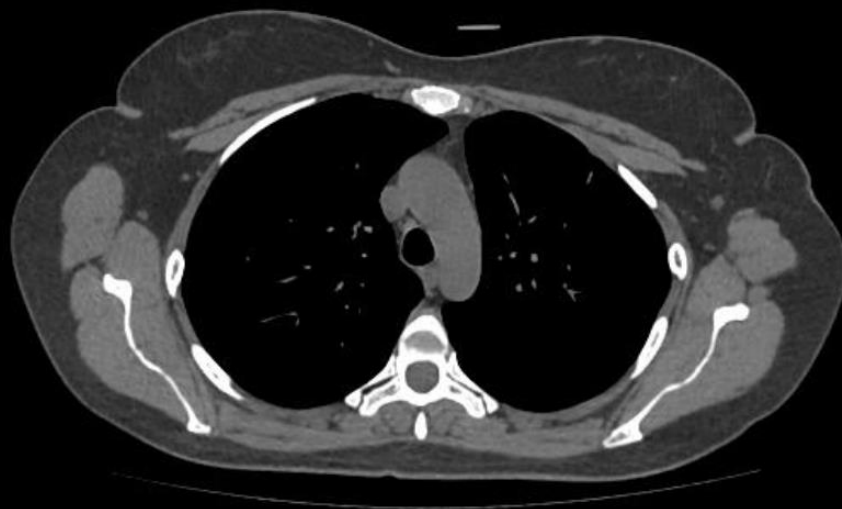




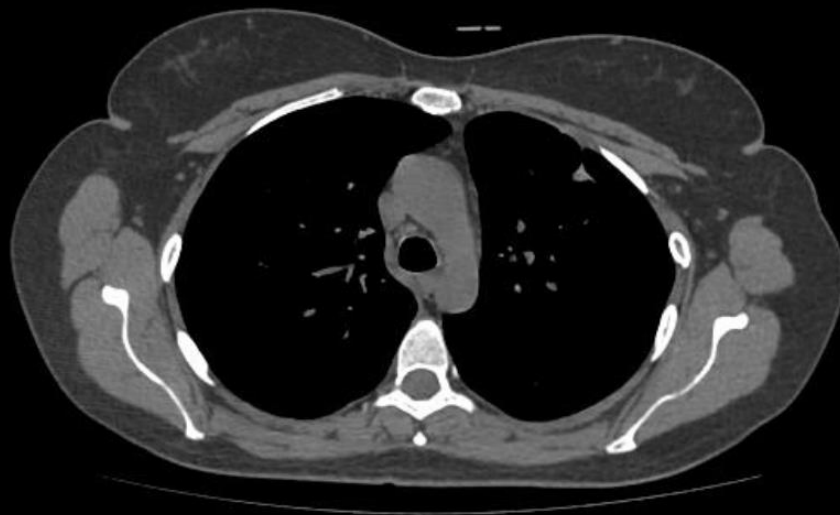












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- 04/01/2022- Exames evidenciam massa cervical posterior esquerda

Programado RT 30 Gy/ 10 fx

Novo ciclo de QT - Aza em jan /22

Leucopenia, plaquetopenia

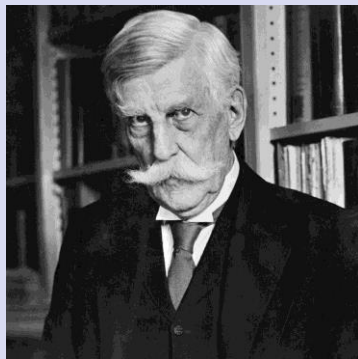
Aguarda melhora laboratorial após transfusão para liberar RT

Paciente interna por Covid 19 com comprometimento respiratório e piora do quadro clínico geral

Óbito 14/02/2022

**"Curar às vezes, aliviar muito frequentemente
e confortar sempre."**

Oliver Wendell Holmes





OBRIGADA!



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