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Hodkgin lymphoma concomitant of tuberculosis, a therapeutic challenge for multidisciplinary management

Lymphome de Hodgkin concomitant d'une tuberculose, un challenge thérapeutique pour une prise en charge pluridisciplinaire

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Abstract

Hodgkin lymphoma (HL) is a disease characterized by a high curability rate, and the treatment benefit-risk balance must be carefully addressed to achieve complete disease control with low risk of long-term toxicities. Most patients are treated with a combination of chemotherapy and radiotherapy, after disease staging and response to treatment evaluated by FDG PET/CT.

We report the case of a 28-year-old patient concomitantly diagnosed of a Hodgkin lymphoma and active tuberculosis. Initial staging was difficult due to pulmonary and abdominal tuberculosis localization that induced FDG PET/CT hypermetabolism. Anti-tuberculosis treatment was first started, allowing secondary an early accurate Hodgkin lymphoma staging by FDG PET/CT. The patient was then treated by chemotherapy and radiotherapy. Helical TomoTherapy® was used with involved site (IS) irradiation volume was performed to decrease the high doses to organs-at-risk (OAR), especially lungs in this context of tuberculosis.

Words: 139

Résumé (français)

Le lymphome de Hodgkin est une pathologie caractérisée par un taux de curabilité élevé, et il est indispensable d'étudier précisément la balance bénéfice-risque des traitements pour obtenir une rémission complète de la maladie avec le minimum de toxicités à long terme. La plupart des patients sont traités par une combinaison de chimiothérapie et de radiothérapie, après une stadification initiale et une évaluation de la réponse au traitement par FDG PET/CT.

Nous rapportons le cas d'un patient de 28 ans, diagnostiqué concomitamment d'un lymphome de Hodgkin et d'une tuberculose active. La stadification initiale a été rendue difficile à cause de localisations pulmonaire et abdominale de la tuberculose, conduisant à un hypermétabolisme au FDG PET/CT. Un traitement anti-tuberculeux a été débuté en premier, permettant une stadification secondaire plus précise du lymphome de Hodgkin avec le FDG PET/CT. Le patient a ensuite été traité par chimiothérapie puis radiothérapie. La tomothérapie hélicoïdale a été utilisée avec pour volumes d'irradiation les sites initialement envahis, pour diminuer les doses aux organes à risque, notamment les poumons dans ce contexte de tuberculose.

Brief communication

Hodgkin lymphoma is a disease characterized by a high curability rate, with a 5-year relative survival close to 84% for all stages (1). Treatment of localized disease is based on chemotherapy and radiotherapy. Benefit-risk balance must be carefully addressed to achieve complete disease control without long-term toxicities (2). The main challenge of radiotherapy is to reduce the risk of second cancer or cardiac disease, which can be achieved by reducing the total dose, reducing treatment volume and using highly performing radiotherapy techniques (3).

The Intensity-Modulated Radiotherapy (IMRT) as the Helical TomoTherapy®, is combining accurate patient positioning, improved homogeneous coverage of target volumes along with a sparing of OAR compared to three-dimensional conformal radiotherapy (3DCRT) for patients with supradiaphragmatic Hodgkin lymphoma (3).

This paper reports the case of a 28-year-old patient concomitantly diagnosed of a Hodgkin lymphoma and active tuberculosis, treated by anti-tuberculosis antibiotherapy, chemotherapy and radiotherapy, after a challenging accurate Hodgkin lymphoma staging by 18F-FDG PET/CT (FDG PET/CT), as previously reported (4). Helical TomoTherapy® was performed to obtain homogeneous coverage of the treatment volume and decrease the doses to organs at risk.

Here, we report the case of a 28-year-old man without any comorbidity, presented a cervical tumefaction with a general alteration, asthenia and hemoptoic sputum. Cervical lymph node biopsy revealed Hodgkin scleronodular lymphoma. Initial CT-scan imaging showed multiple cervical and sus-clavicular bilateral lymph nodes, and mediastinal and right axillary lymph nodes as shown in Figure 1. The CT scan also revealed an alveolo-interstitial

syndrome with a nodular lesion, none evocative of Hodgkin lymphoma (Figure 1). In this context, a bronchoscopy with bronchoalveolar lavage was performed and revealed the presence of mycobacterium tuberculosis, in favor of an active tuberculosis.

A first FDG PET/CT (General Electric Discovery ™710 ELITE (General Electric Healthcare) with time of flight (TOF) technology) confirmed an intense hypermetabolism of cervical and sub-clavicular lymph nodes. Interestingly, an hypermetabolism of the alveolo-interstitial syndrome associated with mediastinal lymph nodes was observed, along with an hypermetabolism of the right colon (Figure 1, Figure 2A). A hypermetabolic sub-diaphragmatic node, not visible on the CT-scan, was also observed, raising suspicion of below diaphragmatic Hodgkin lesion (Figure 2A). A biopsy of colon confirmed digestive tuberculosis localization, but peri-colonic lymph nodes could not be biopsied due to bleeding risk.

The stage of Hodgkin lymphoma (HL) was equivocal between stage II (only above diaphragm lymph nodes) or stage III (above and below diaphragm lymph nodes). After multidisciplinary discussion it was decided to start anti-tuberculosis quadruple drugs antibiotherapy (isoniazid, rifampin, pyrazinamide, and ethambutol). Secondary, a FDG PET/CT performed after one month of anti-tuberculosis treatment (Figure 2B) showed persisting hypermetabolism of cervical and sub-mandibular bilateral and right axillary lymph nodes (SUVmax 6.9 before antibiotherapy vs 10.9 after antibiotherapy), but a decreased metabolism of pulmonary (SUVmax 5.4 before antibiotherapy vs 2 after antibiotherapy), mesenteric and colic (SUVmax 10.9 before antibiotherapy vs 7.4 after antibiotherapy) tuberculosis localization. A complete metabolic response of infra diaphragmatic lymph nodes was achieved (SUVmax 6.5 before antibiotherapy vs none after antibiotherapy), making it likely to be due to tuberculosis (Figure 2B).

Finally, Hodgkin lymphoma was staged II Aa, unfavorable group (>4 lymph nodes groups). FDG PET/CT performed after 4 cycles of ABVD (doxorubicin bleomycin–vinblastine–dacarbazine) showed a complete metabolic response of lymphoma (Deauville 2 criteria) and a complete disappearance of tuberculosis initial localization.

Involved site (IS) radiotherapy of 30 Gy in 15 fractions was then performed (cervical and sub-clavicular bilateral, right axillary, hilar and mediastinal localization), as shown in Figure 3, while the patient was still under bitherapy for anti-tuberculosis treatment. The lungs V20 was 11.3%, and mean cardiac dose was 1.4 Gy. No early toxicity was observed. Anti-tuberculosis antibiotherapy was given for six months. Currently, 30 months after the end of the treatment of both Hodgkin lymphoma and tuberculosis, the patient is asymptomatic, in complete remission without any late treatment related toxicity or tuberculosis relapse (Figure 2C).

Hodgkin lymphoma is a curable disease after modern treatment by chemotherapy and radiotherapy (1). The main challenge is to reduce long term toxicity of both chemotherapy and radiotherapy. The modern HL management closely relies an accurate staging using FDG PET/CT currently considered as a standard for staging, assessment of the treatment response and in some cases: follow-up of HL (5). The FDG PET/CT is not specific of malignancies and that hypermetabolism can be observed in inflammatory process (6,7). This case is a perfect example of the use of new imaging techniques as previously reported to do the differential diagnosis (4). At the same time, this case represents also an example of the interest of multidisciplinary discussion and management of these rare cases.

Tuberculosis treatment was decided in collaboration with infectiology specialists and relied on a quadruple drug antibiotherapy (isoniazid, rifampin, pyrazinamide, and ethambutol) for 2 months, then 4 months with isoniazid and rifampicin. No drug interaction

with the chemotherapy was reported with rifampicin (a powerful enzymatic inductor), allowing clinicians to start chemotherapy despite tuberculosis treatment. Isoniazid and rifampicin concentations were not monitored during chemotherapy course since the patient did not experience any grade 3/4 hematological and non-hematological complications. Tuberculosis treatment resulted in a rapid decrease of abdominal hypermetabolism, allowing distinction between HL and tuberculosis nodes, which helped to stage accurately HL. Concomitant anti-cancer-therapy treatment and anti-tuberculosis treatment has already been proved effective and safe for treating cancer patients with active tuberculosis (8).

However, the choice of radiotherapy technique was also challenging in this context of pulmonary tuberculosis. Considering the risk of tuberculosis lung sequelae, avoiding to give high doses to lungs was crucial and was achieved by adapting the radiotherapy technique (3,9). Several studies proved an improved target volumes coverage along with a better sparing of some organs at risk with Intensity-Modulated Radiotherapy (IMRT), compared to three-dimensional conformal radiotherapy (3DCRT) (10). The IMRT can be delivered using HT as previously reported (9). On the other hand, treatment volumes were adapted using "involved-site" (IS) radiotherapy, following the ILROG Guidelines (11).

In conclusion, in a context of concomitant Hodgkin lymphoma and tuberculosis, accurate staging is crucial for optimal treatment of HL, which was possible with repeated FDG PET/CT imaging. An individualized radiotherapy management was also essential to decrease dose to OAR and obtain perfect coverage of the treatment volume.

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Informed consent statement

Written informed consent was obtained from the patient for publication of this case report, including accompanying images.

Figure legends

Figure 1 (English)

A and B : CT-scan imaging at diagnosis (A) and after completion of both TB and Hodgkin lymphoma (HL) treatment (B).

(A1-A2) Multiple homogenous left sus-clavicular nodes (red arrow A1) and medium and anterior mediastinal nodes (red arrow A2).

(A3-A4) Parenchymal window with linear and irregular opacities associated with bronchectasis (red arrow A3) and multiple centrolobular micronodules with a budding tree aspect (red arrow A4).

(A5-A6) coronal and sagittal reconstruction in maximum Intensity Projection (MIP), with bronchial and bronchiolar lesions, exclusively in the apical segment of the upper right lobe (arrow in A5) and apical segment of inferior right lobe (arrow in A6).

(B1-B2) Post-therapeutic aspect with disappearance of initial nodes.

(B3-B6) Lung sequelae after tuberculosis treatment on parenchymal window and coronal and sagittal reconstruction

Figure 1 (Français)

A et B : Images de scanner au diagnostic (A) et après traitement à la fois de la tuberculose et du lymphome de Hodgkin (B)

(A1-A2) Multiples ganglions sous-claviculaires gauches (flèche rouge A1), et ganglions du médiastin moyen en antérieur (flèche rouge A2).

(A3-A4) Fenêtre parenchymateuse, avec des opacities linéaires et irrégulières associées à des bronchectasies (flèche rouge A3) et de multiples micrnodules centrolobulaires avec un aspect d'arbres bourgeonnant (flèche rouge A4).

(A5-A6) reconstruction sagittale et coronale en Intensité de Projection maximale (MIP), avec des lesions bronchiques et bronchiolaires, exclusivement du segment apical du lobe supérieur droit (fleche en A5), et du segment apical du lobe inférieur droit (fleche en A6).

(B1-B2) Aspect post-thérapeutique avec disparition des ganglions initiaux.

(B3-B6) Séquelles pulmonaires après traitement de la turberculose en fenêtre parenchymateuse et en reconstruction sagittale et coronale.

Figure 2 (English)

^{18}FDG PET/CT MIP (maximum intensity projection) and fused PET/CT (subclavicular, pulmonary and abdominal localization) of initial staging (A), one month after anti-tuberculosis (TB) treatment (B) and after completion of both TB and Hodgkin lymphoma (HL) treatment (C).

(1) Hypermetabolism of cervical, mediastinal and axillary lymph nodes, as well as pulmonary and colonic uptake with mesenteric lymph nodes (white arrow).

(2) One month after initiation of anti-TB antibiotherapy, with a decrease of pulmonary, colonic and mesenteric lymph nodes uptake, but increased uptake of above diaphragm nodes.

(3) Complete metabolic response after HL and TB treatment, with TB lung sequelae.

Figure 2 (Français)

Images du ^{18}FDG PET/CT MIP (intensité de projection maximale) et du PET/CT fusion (localization sous-claviculaire, pulmonaire et abdominale) lors de la stadification initiale (A), un mois après le début du traitement anti-tuberculeux (B) et après traitement à la fois de la tuberculose et du lymphome de Hodgkin (LH) (C)

(1) Hypermetabolisme des ganglions cervicaux, médiastinaux et axillaires, ainsi que pulmonaire et colique avec des ganglions mésentériques (flèche blanche).

(2) Un mois après le début du traitement anti-tuberculeux, avec une diminution de l'hypermétabolisme pulmonaire, colique et des ganglions mésentériques, mais une augmentation de l'hypermétabolisme des ganglions sus-diaphragmatiques.

(3) Réponse métabolique complete après traitement anti-tuberculeux et traitement du lymphoma de Hodgkin, avec séquelles pulmonaires de tuberculose.

Figure 3 (Anglais)

Tomotherapy plan with isodoses.

(A) Isodose from 15 Gy (50 % of the dose of PTV 30 Gy) to 32,5 Gy (107% of the dose of PTV 30 Gy). Colour-wash with high doses in red and low doses in blue.

(B) Isodose from 28,5 Gy (95% of the dose of PTV 30 Gy) to 32,5 Gy (107% of the dose of PTV 30 Gy). Colour-wash with high doses in red and low doses in blue.

(C) 3D-representation of CTV

(4) Dose-volume histograms of the Tomotherapy plan, with organ-at-risk doses. Constraint was maximal on lungs (green and purple).

Figure 3 (Français)
Plan de traitement de tomothérapie avec les isodoses.

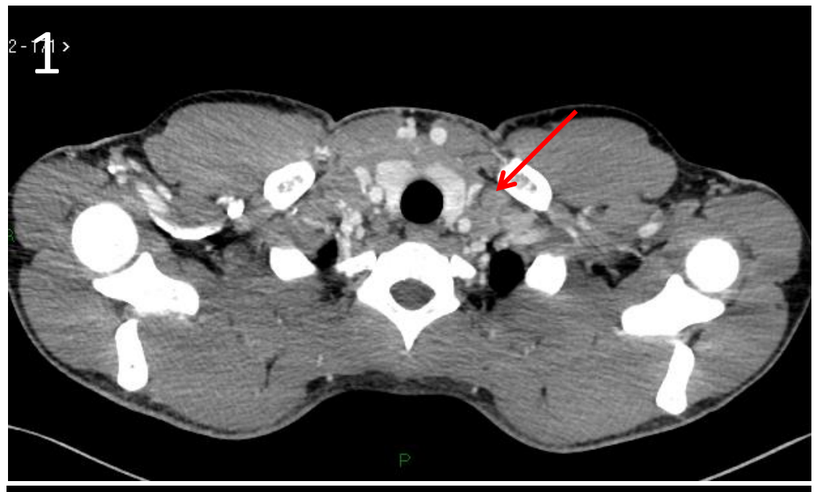
(A) Isodose de 15 Gy (50 % de la dose du PTV 30 Gy) à 32,5 Gy (107% de la dose du PTV 30 Gy). Les fortes doses sont en rouge et les faibles doses en bleu.

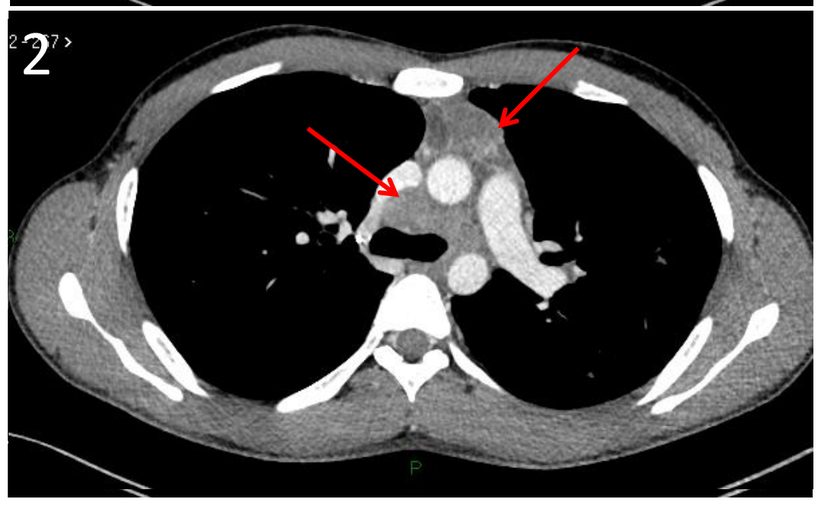
(B) Isodose de 28,5 Gy (95% de la dose du PTV 30 Gy) à 32,5 Gy (107% de la dose du 30 Gy). Les fortes doses sont en rouge et les faibles doses en bleu.

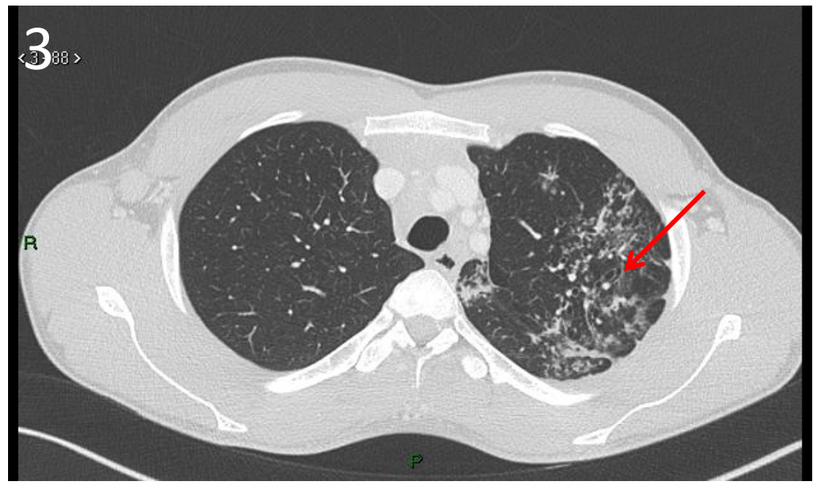
(5) Représentation 3D du CTV.

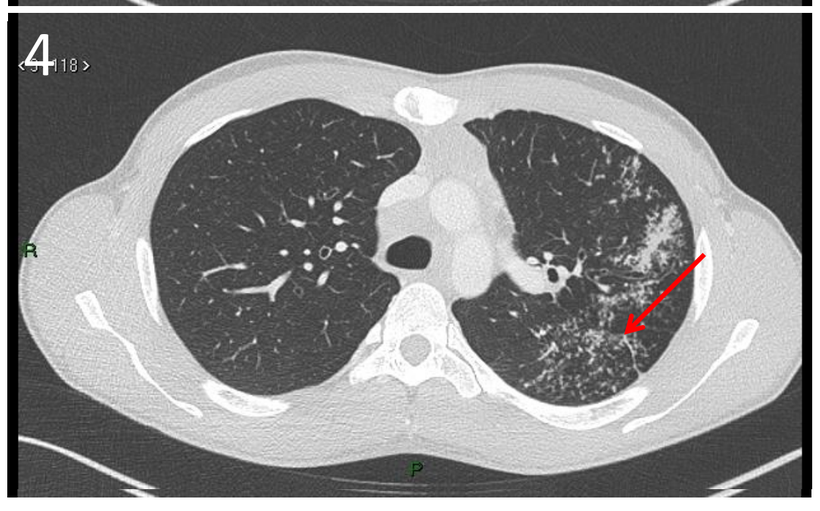
(6) Histogrammes dose-volume du plan de traitement de tomothérapie, avec les doses aux organes à risque. Les contraintes étaient maximales sur les poumons (vert et violet).

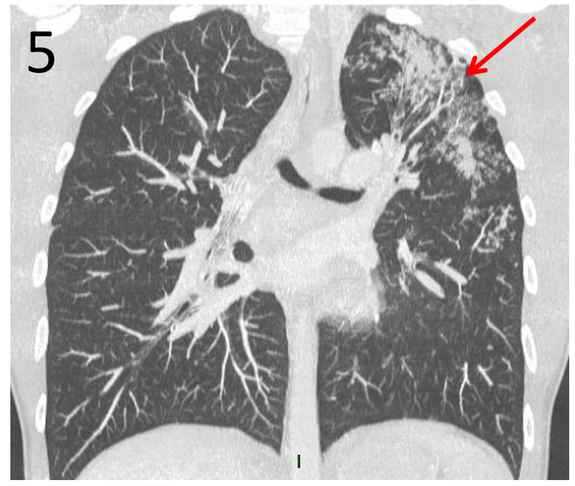
A

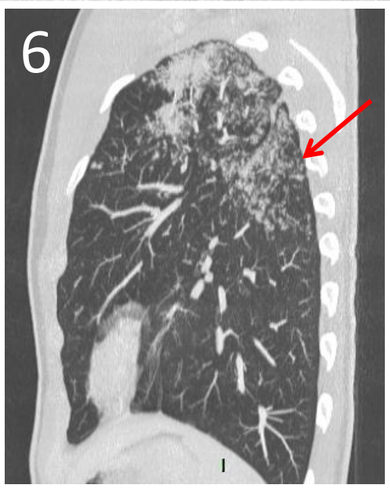




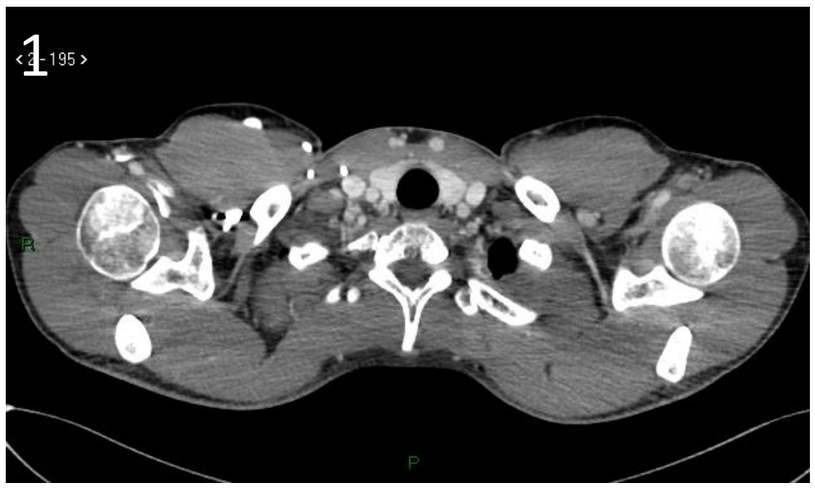


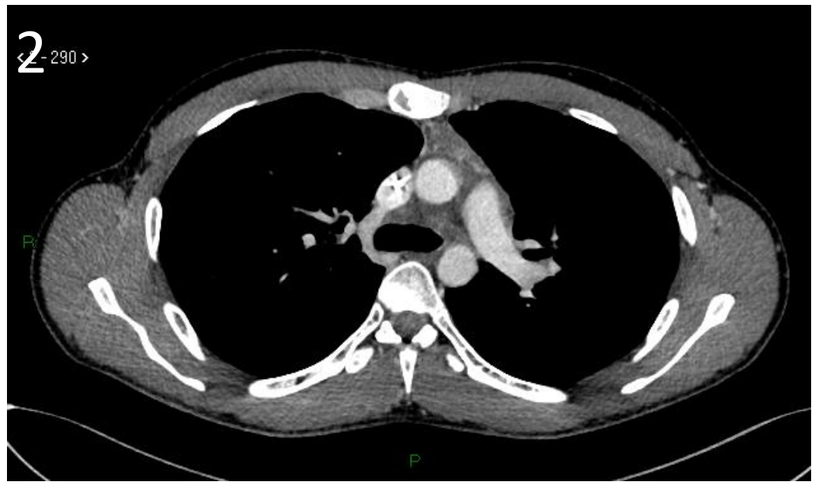


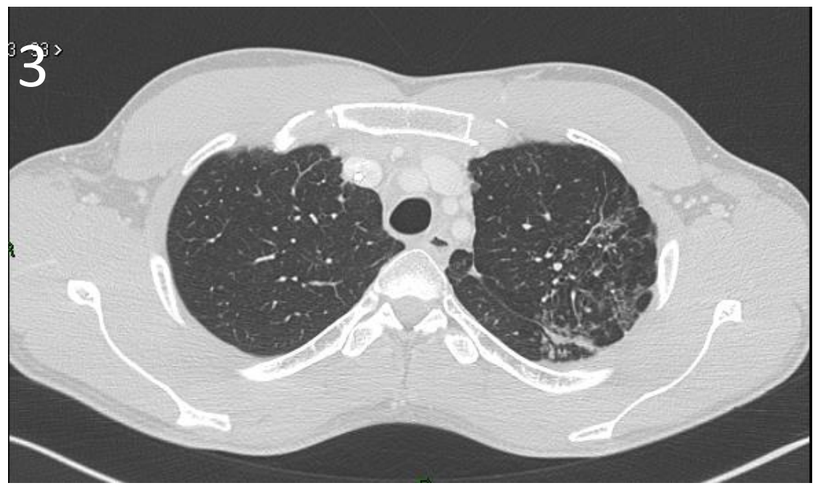


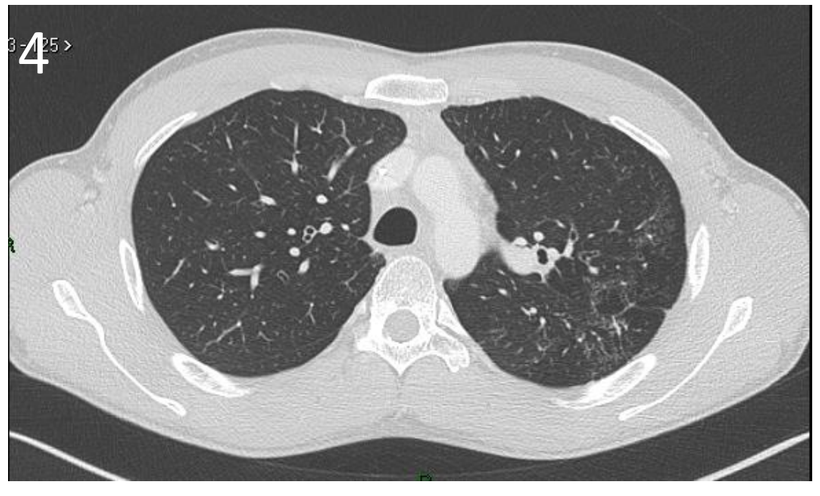


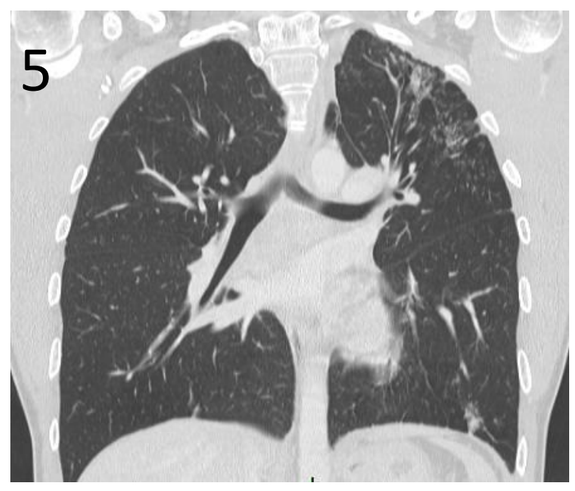
B

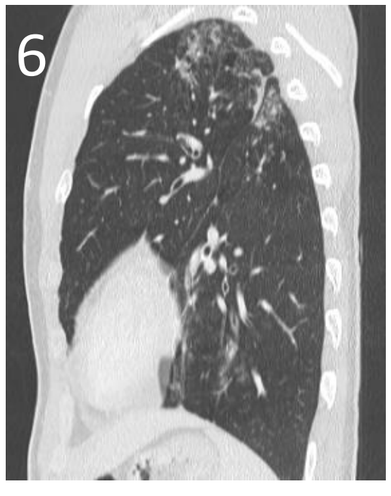


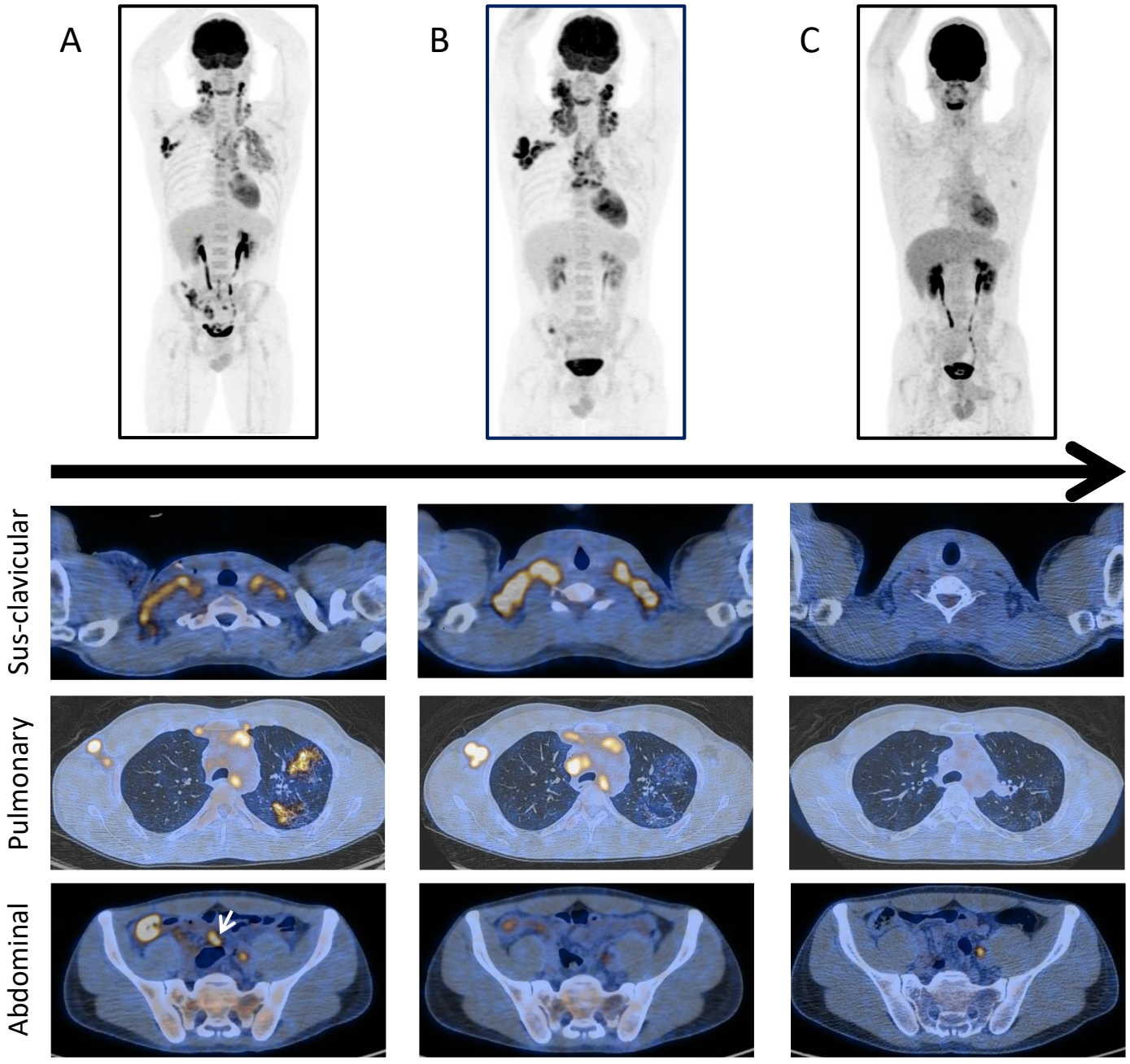




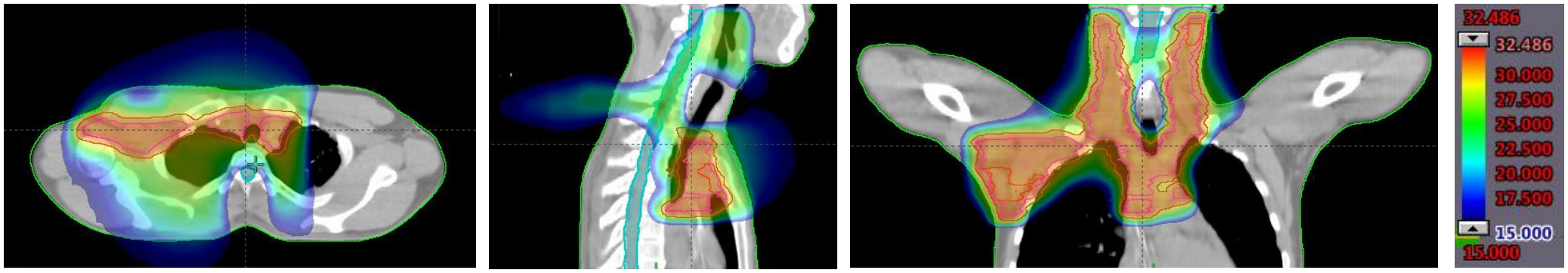




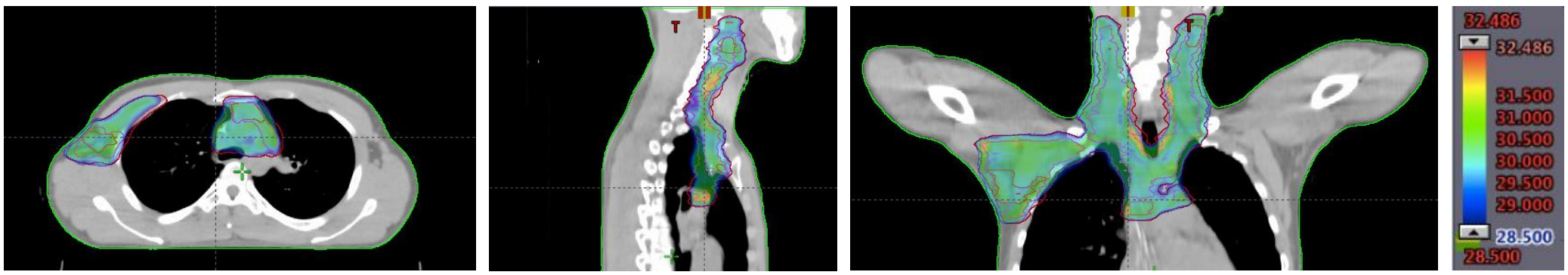



A
B
C
Sus-clavicular
Pulmonary
Abdominal
Before TB treatment
One month after TB treatment
After TB and HL treatment

A


32.486
32.486
30.000
27.500
25.000
22.500
20.000
17.500
15.000
15.000

B


32.486
32.486
31.500
31.000
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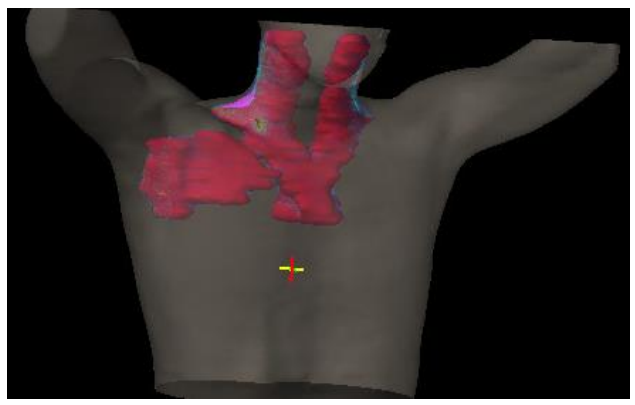
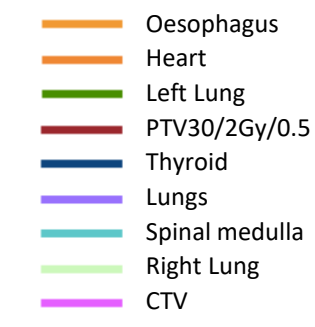
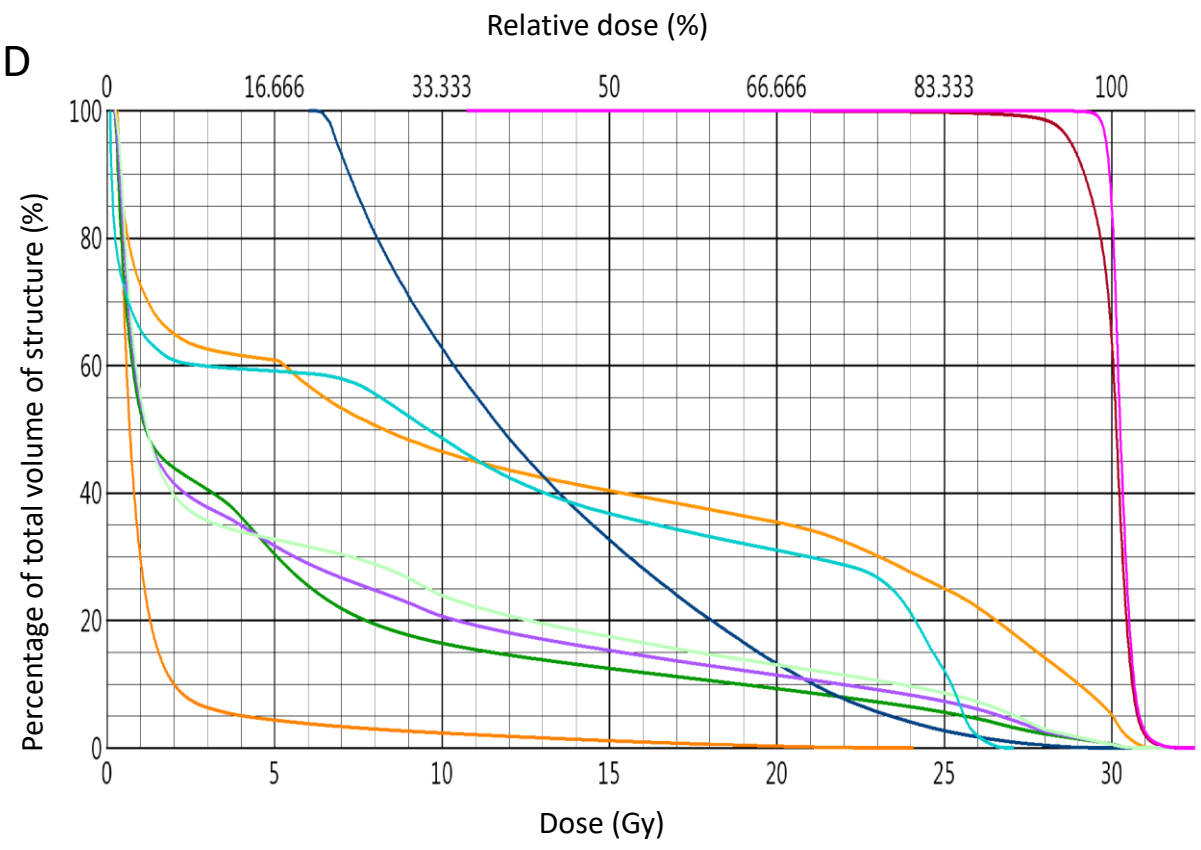
30.000
29.500
29.000
28.500
28.500

C




Oesophagus
Heart
Left Lung
PTV30/2Gy/0.5
Thyroid
Lungs
Spinal medulla
Right Lung
CTV

D


Relative dose (%)
0
16.666
33.333
50
66.666
83.333
100
100
80
60
40
20
0
Percentage of total volume of structure (%)
0
5
10
15
20
25
30
Dose (Gy)