





A case of primary metastatic leiomyosarcoma

Mikael Eriksson

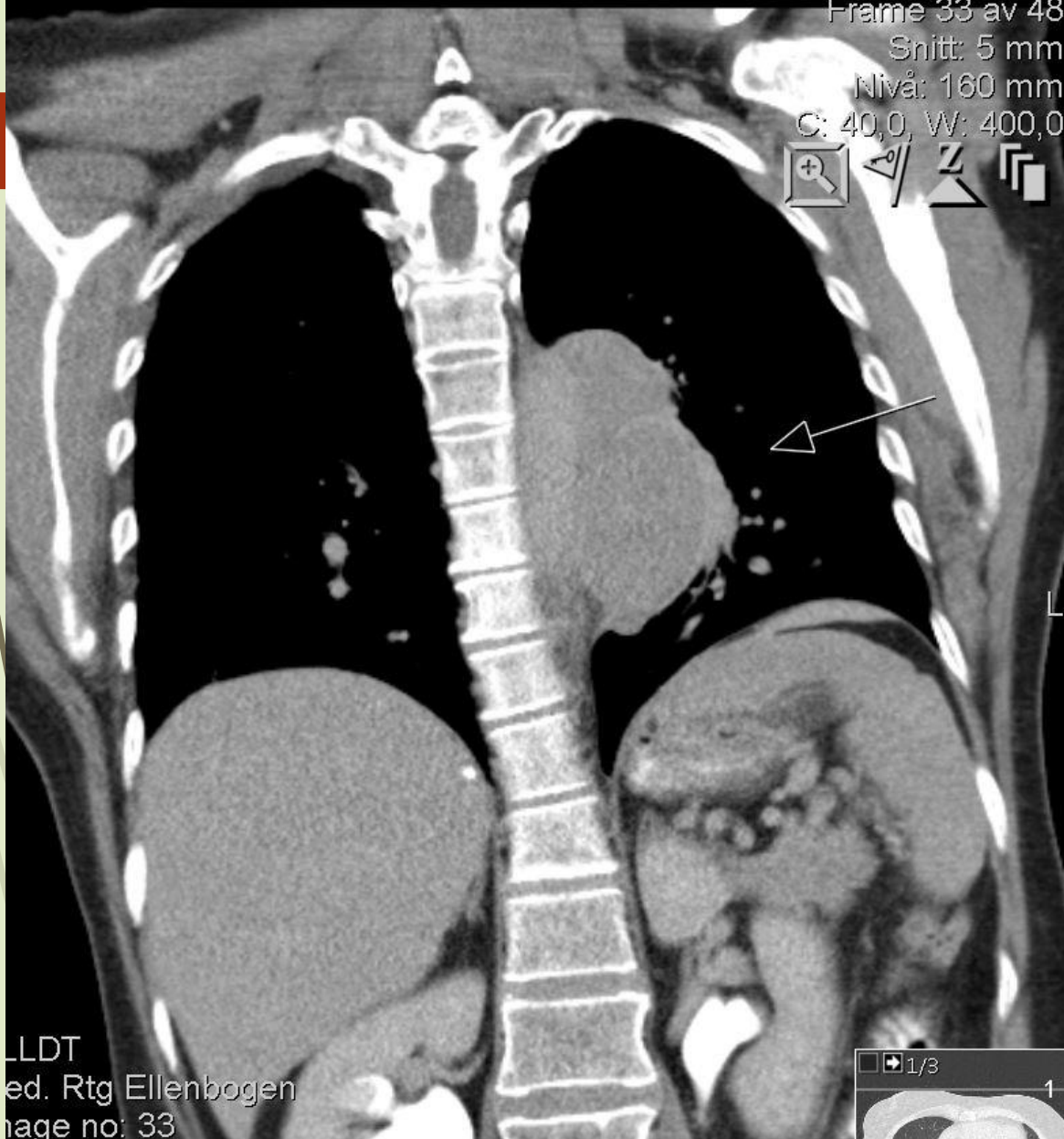
SPAEN Annual Conference

1-3 February 2019, Athens

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- ▶ At diagnosis 60-year old female from Bosnia where she lost her husband and oldest son during the massacre in Srebrenica during the Bosnia war in the 90-ies
 - ▶ Developed a posttraumatic depression, in periods treated with anti-depressants after arrival to Sweden after the millennium shift
 - ▶ About 2007 a period of abdominal discomfort; colonoscopy showed inflammatory changes but no treatment was given, improved spontaneously
 - ▶ Otherwise earlier healthy

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- During spring 2013 increasing back pain.
 - She was seeking medical care at the primary health centre several times during a year – referred to physiotherapy and received analgesics and anti-inflammatory drugs; no X-ray done
 - October 2014 severely aggravated pain; primary health centre then referred her to X-ray of lumbar spine and pelvic bone → arthrosis and degenerative changes
 - Finally a CT scan was ordered which showed a large tumour in the lower lobe of the left lung growing into mediastinum; furthermore a destruction in vertebra L:4 extending into a soft part tumour
 - A confirmatory PET scan showed pathological metabolism in those two sites and also in a smaller lesion in right pelvic bone

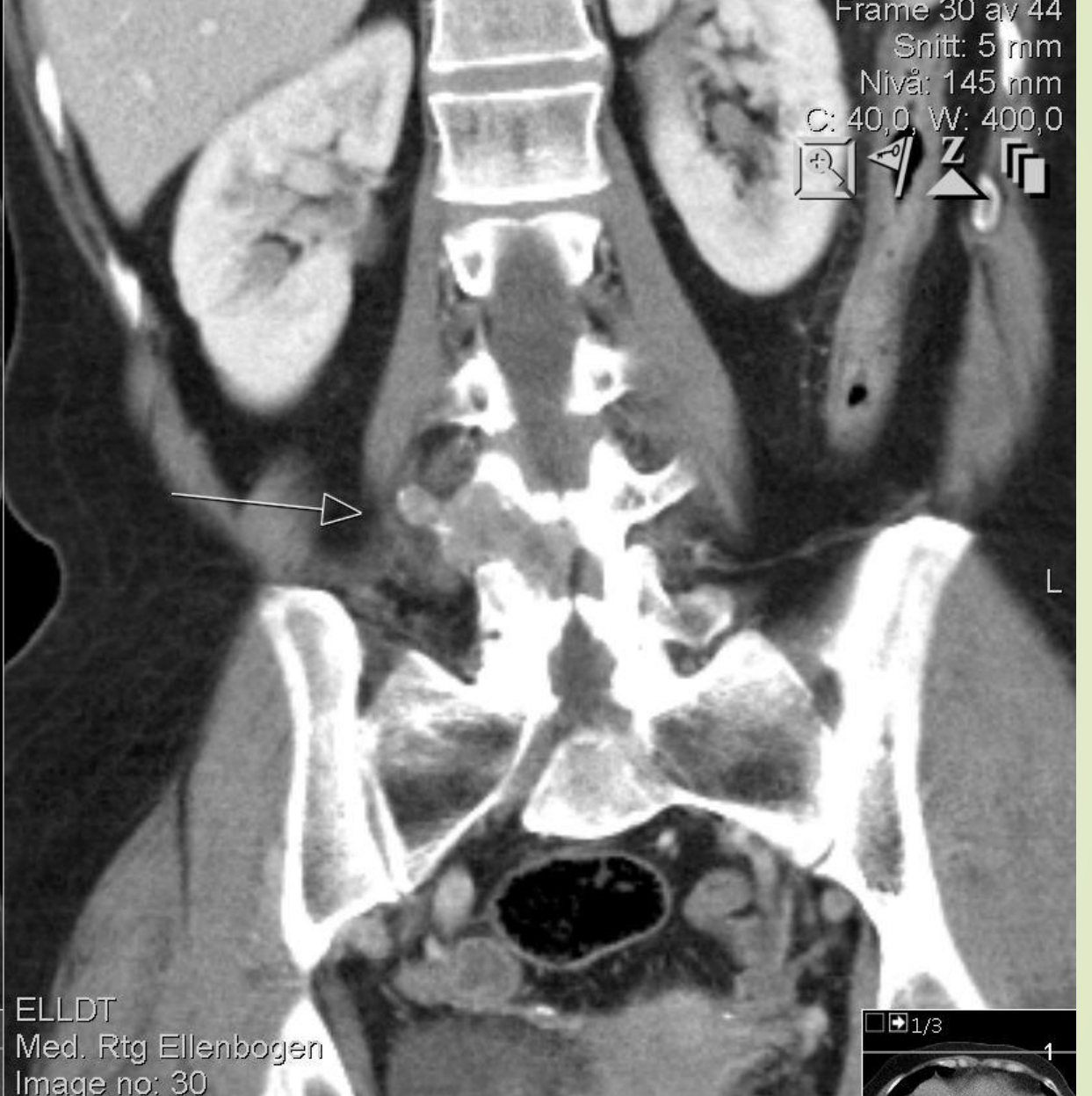
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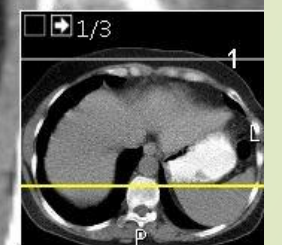
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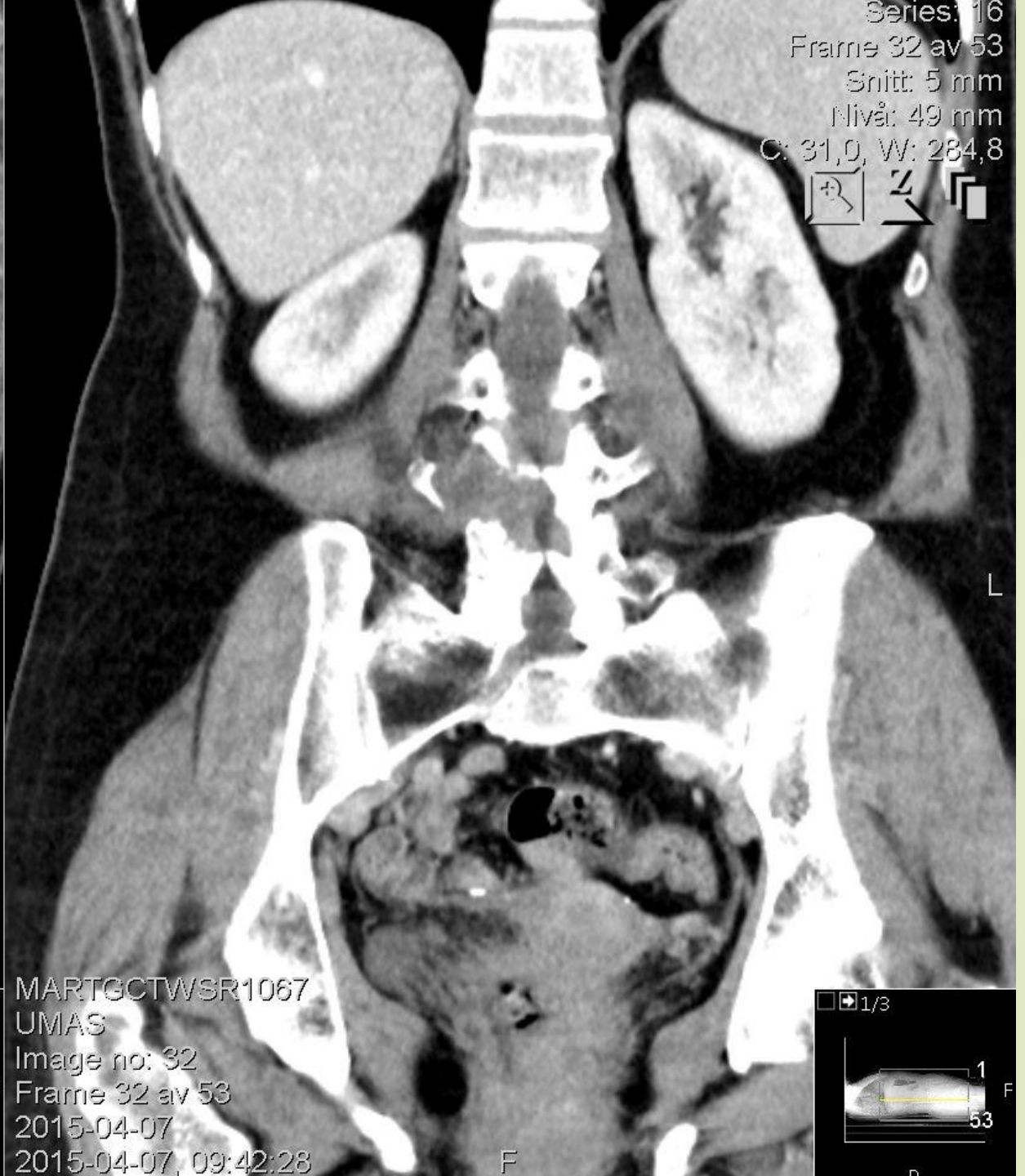
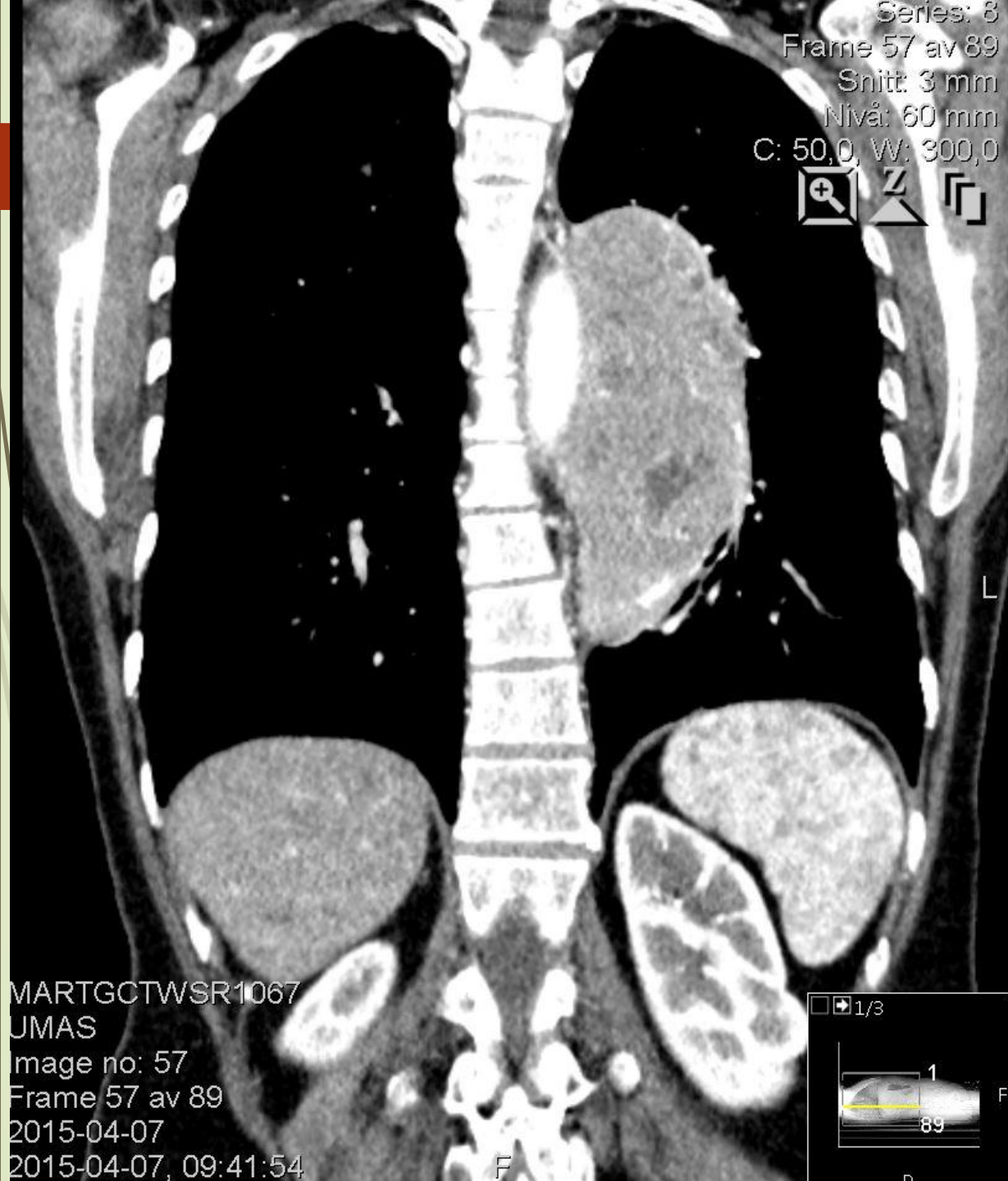
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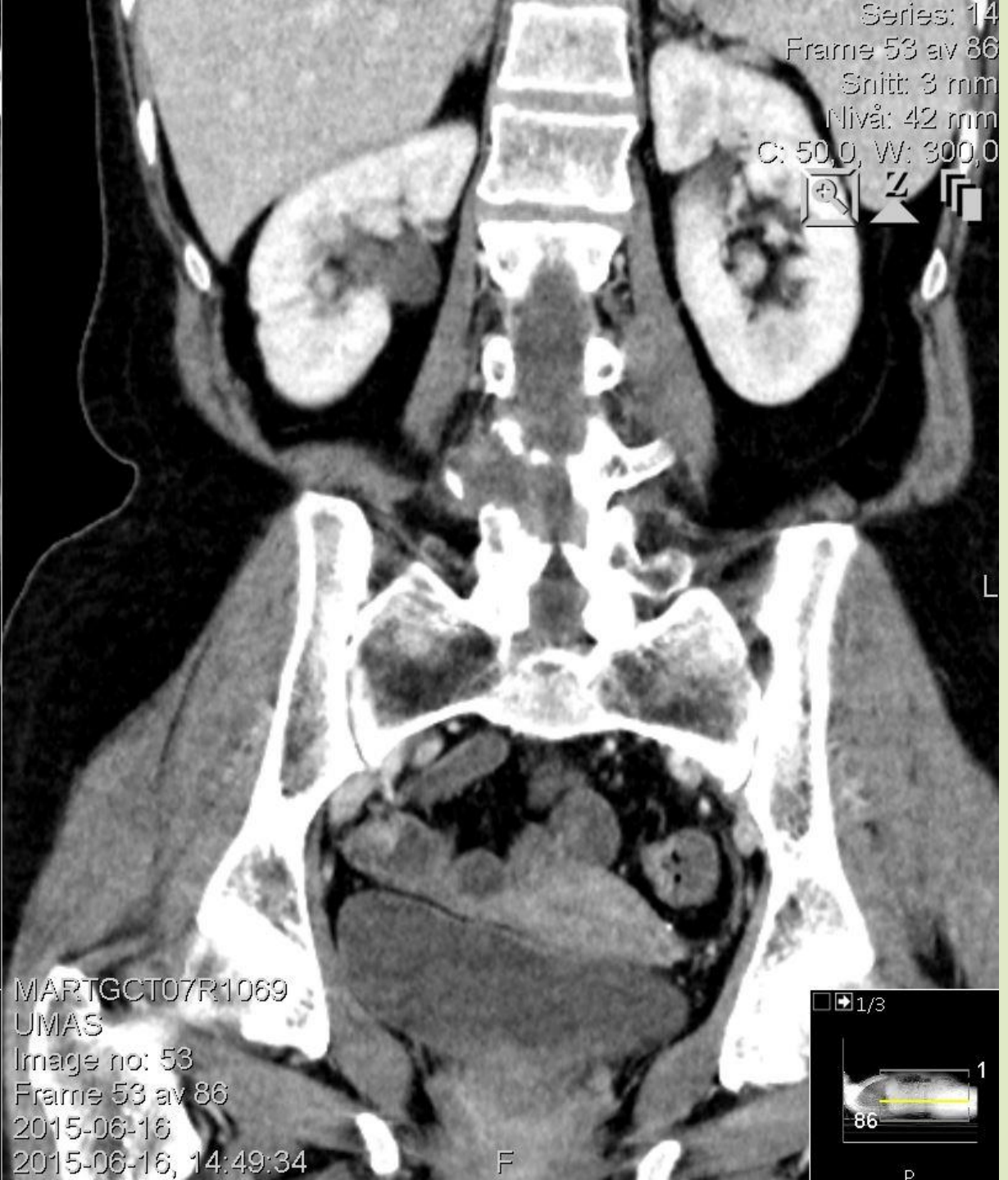
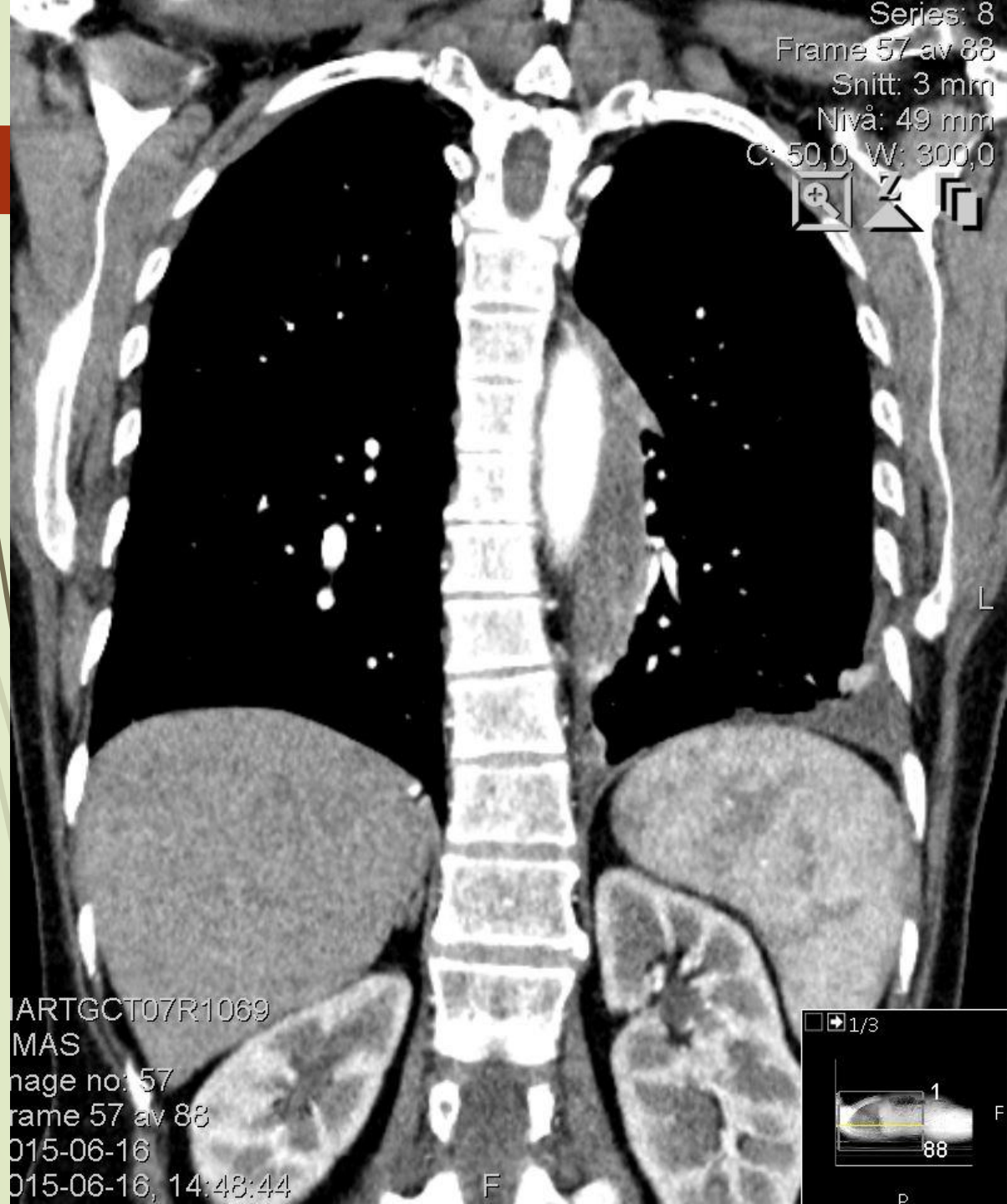
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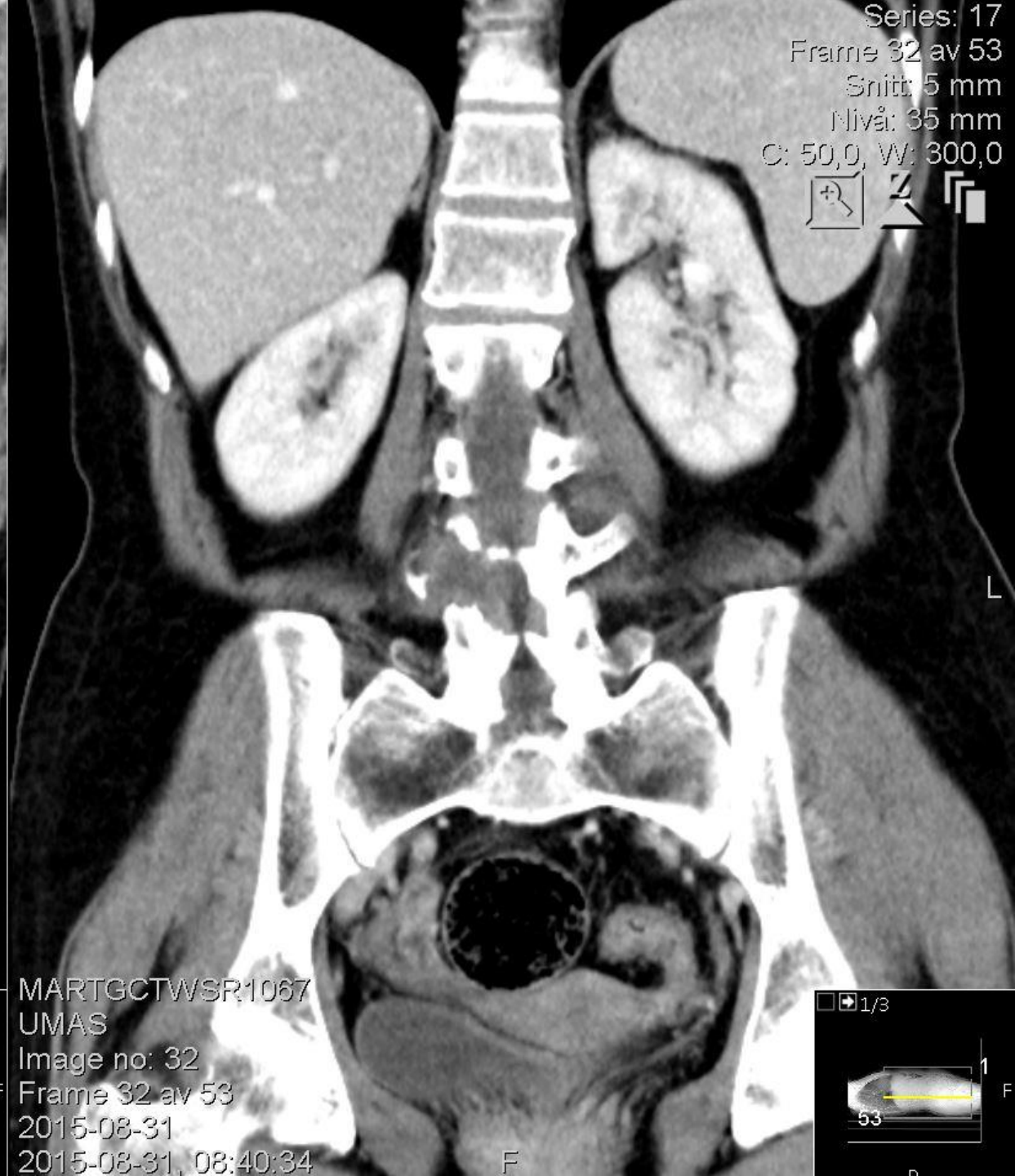
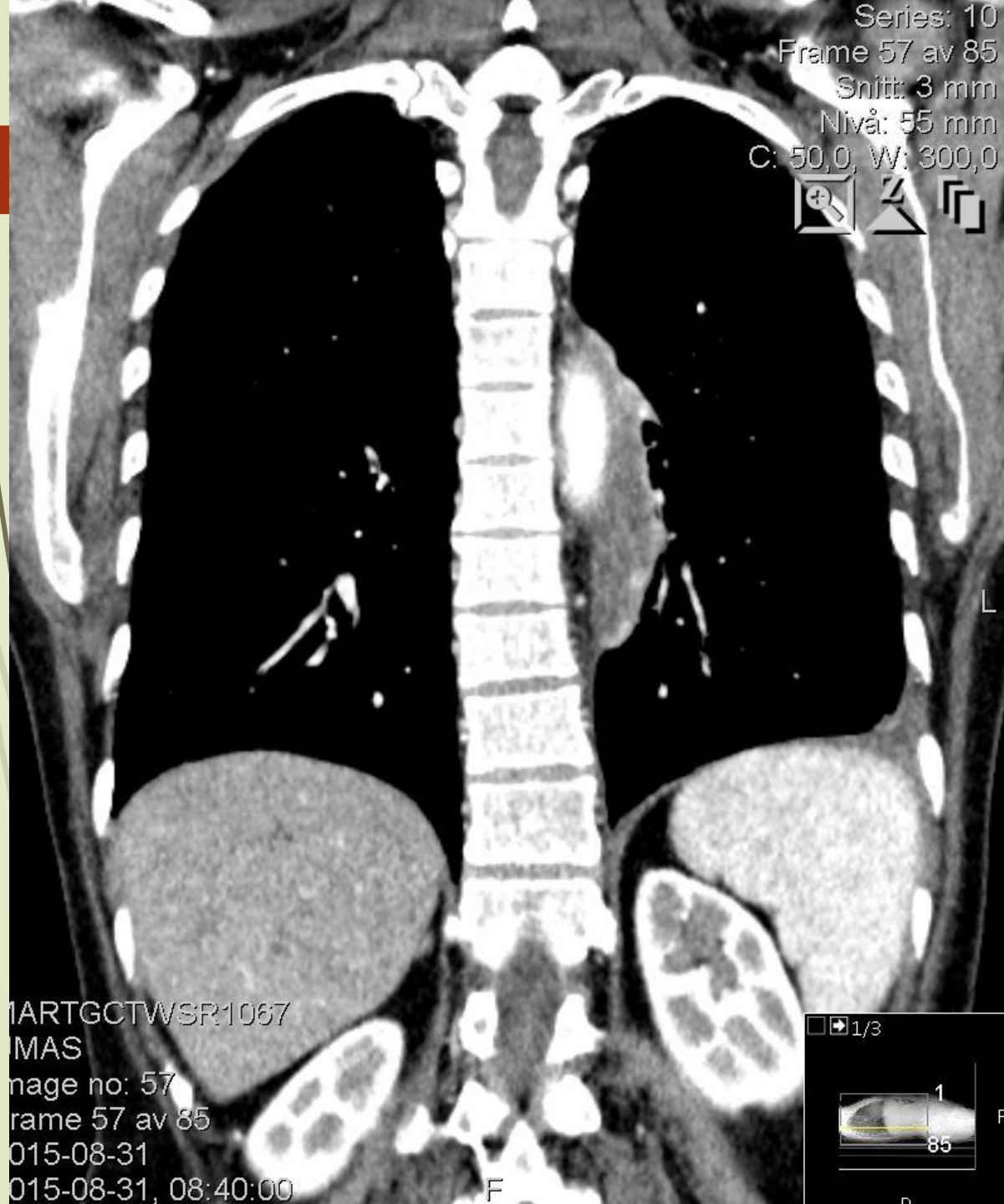
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- In February 2015 radiotherapy was given against the two skeletal metastases to relieve pain (20 Gy/5 fractions)
 - In early March 2015 a core needle biopsy was performed from the lung tumour → pathological diagnosis: pleomorphic leiomyosarcoma
 - Referred to the Sarcoma oncology section in late March, a new baseline CT was made April 7, and chemotherapy started at April 13





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- ▶ Doxorubicin + dacarbazine
 - ▶ After first cycle neutropenic fever, nausea, anaemia and fatigue, but through transfusion and other supportive measures soon improved
 - ▶ After two cycles generally improved, less fatigue and pain
 - ▶ After cycle 3, an evaluating CT scan was performed

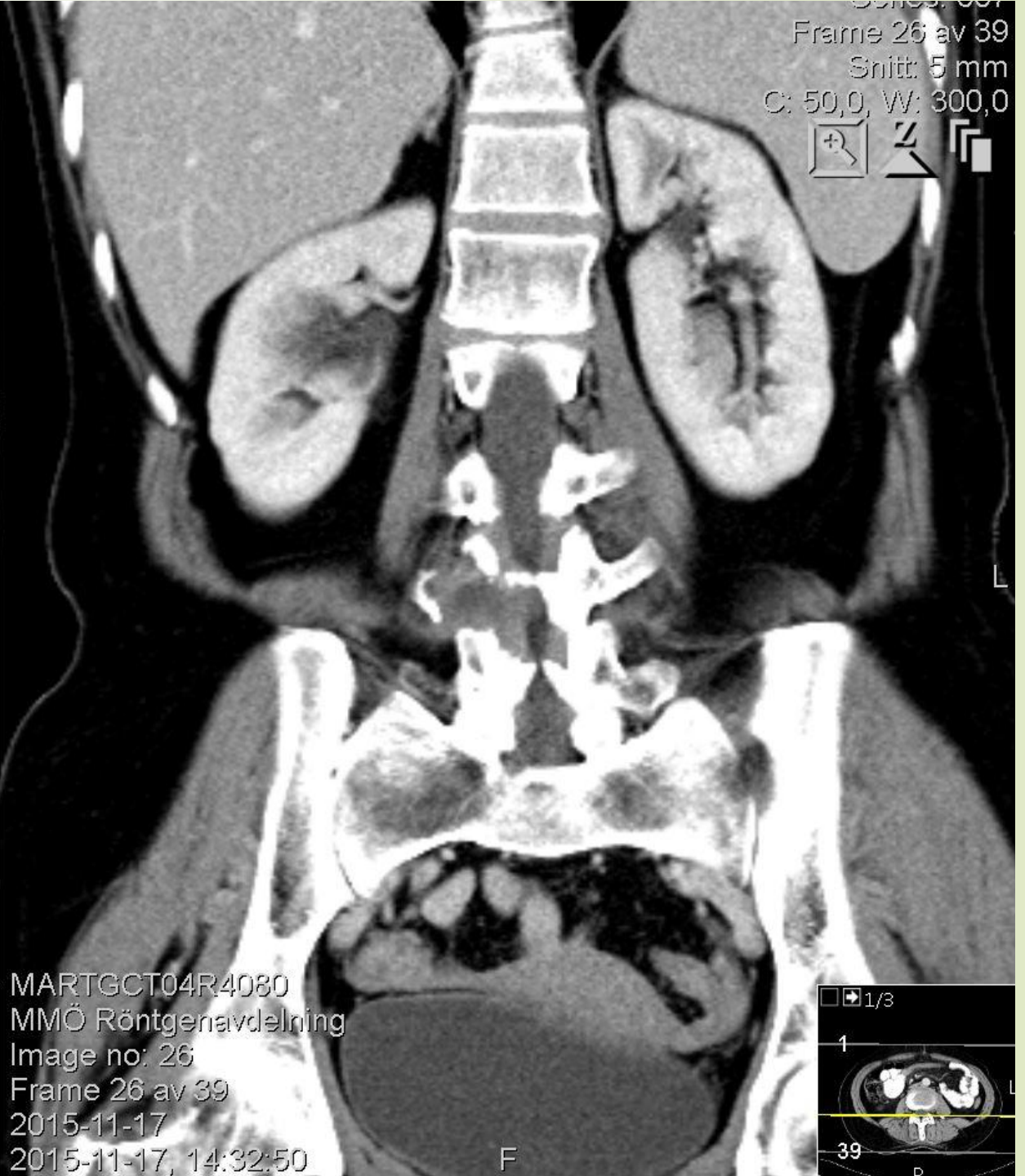
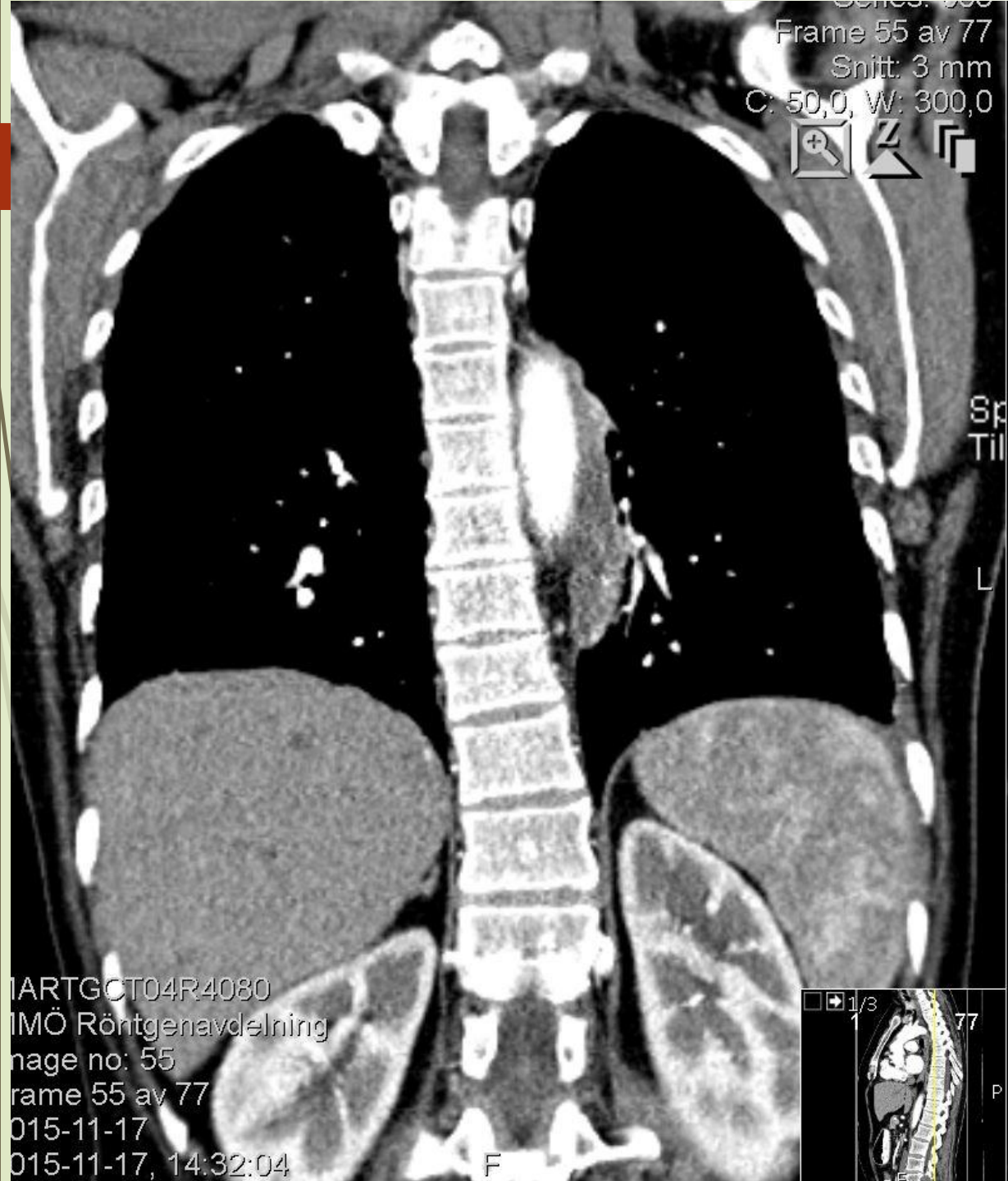



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- Thus a very good regression of the thoracic tumour
 - Metastasis in lumbar spine stable
 - Remaining back pain
 - Received a radiotherapy re-treatment to the spine (8 Gy x 1)
 - Chemotherapy continued with doxorubicin – dacabazine cycles 4-6
 - Tolerated treatment rather well with some supportive care, e.g., a new transfusion between cycle 5 and 6
 - New CT was done after cycle 6





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- ▶ Thus further good regression of the thoracic tumour, whereas the spine metastasis is stable
 - ▶ Decreased back pain and lowered doses of analgetics
 - ▶ After 6 cycles, the cumulative dose of doxorubicin is 450 mg/m²
 - ▶ What to do next?
 - continue with the same treatment if cardiac function is good?
 - change to other therapy?
 - treatment pause and follow-up until progression?

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- ▶ We decided to switch to other chemotherapy to:
 - not adventure heart function
 - overcome potential evoking resistance
 - ▶ Started with gemcitabine + dacarbazine in September 2015 according to the schedule suggested by a study from GEIS (but with 21 days cycles instead of 14)
 - ▶ The regimen was very well tolerated
 - ▶ New CT scan after 4 cycles



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- Further regression was seen
 - Received two further cycles up to a total of 6
 - Tolerated the treatment excellent
 - Strong analgesics could be totally stopped
 - New CT scan after 6 cycles showed stable disease
 - What to do now?
 - change to other therapy?
 - treatment pause and follow-up until progression?

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- ▶ We thought it was reasonable to make a break after in total 12 cycles of chemotherapy during 8 months
 - ▶ Close follow-up was planned
 - ▶ Next CT scan in late March 2016: stable disease
 - ▶ In June 2016, still stable CT scan, but some worsening again of back pain corresponding to the affected lumbar spine
 - ▶ Without any certain signs of progression, she received once more palliative radiation in August 2016, with relief of pain after some weeks

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- ▶ Further follow-up with CT scan:
 - September 2016: stable
 - January 2017: stable
 - June 2017: stable
 - October 2017: stable
 - April 2018: some further regression!
 - October 2018: stable
 - Next is planned February 6, 2019



Lessons from this case

- ▶ Leiomyosarcoma (LMS) confirmed as a chemosensitive disease
- ▶ In metastatic LMS, however, one line of chemotherapy is seldom enough
- ▶ Usual strategy in many centres: give one line and if good result, wait and see until progression → new chemotherapy
- ▶ If patient tolerate treatment well, it may be reasonable to try to overcome resistance by giving subsequent different regimens
- ▶ Is this patient “cured”? Impossible to say, but long treatment-free period anyway very beneficial for the patient




A case of epithelioid sarcoma

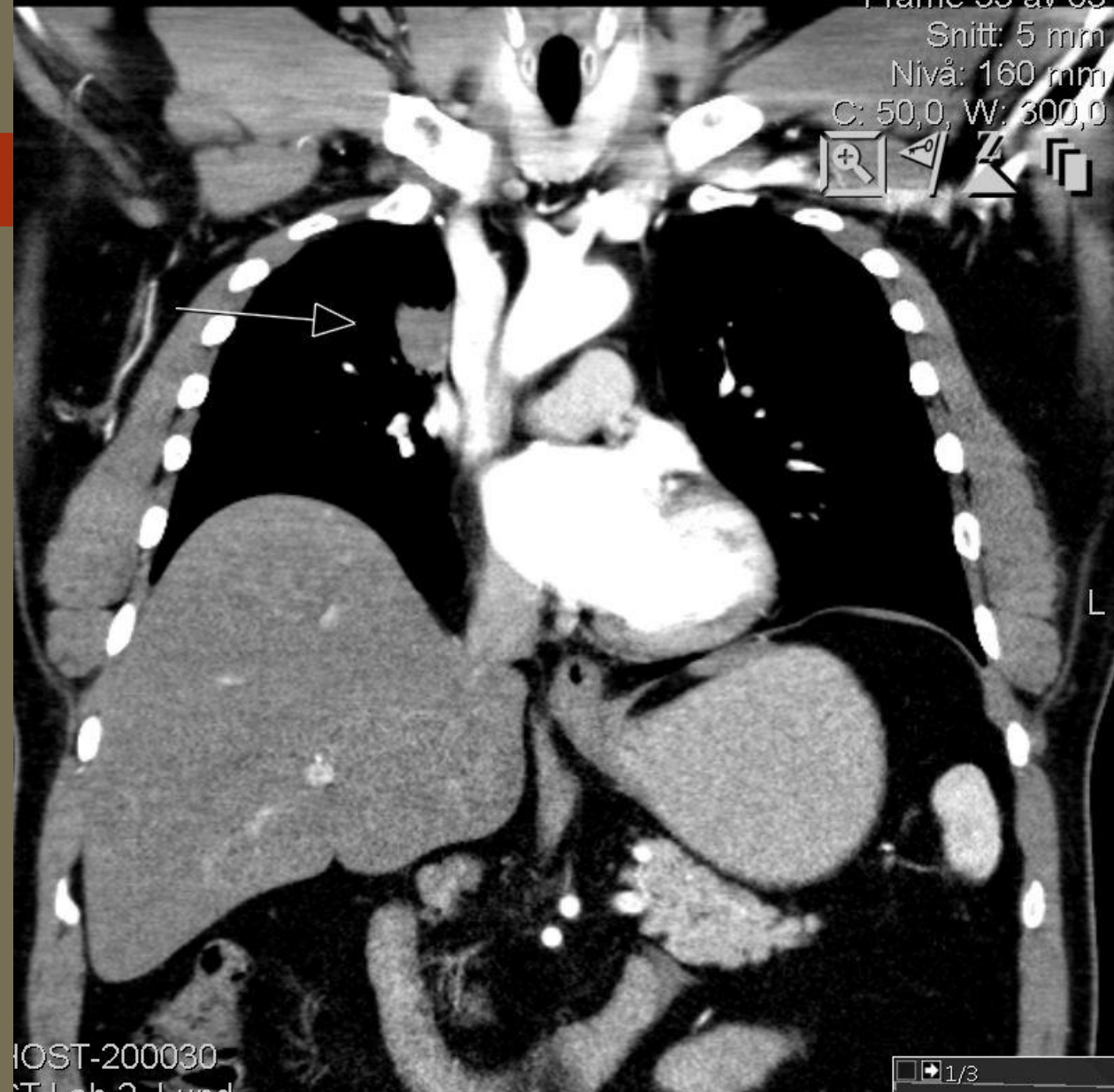
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Epithelioid sarcoma

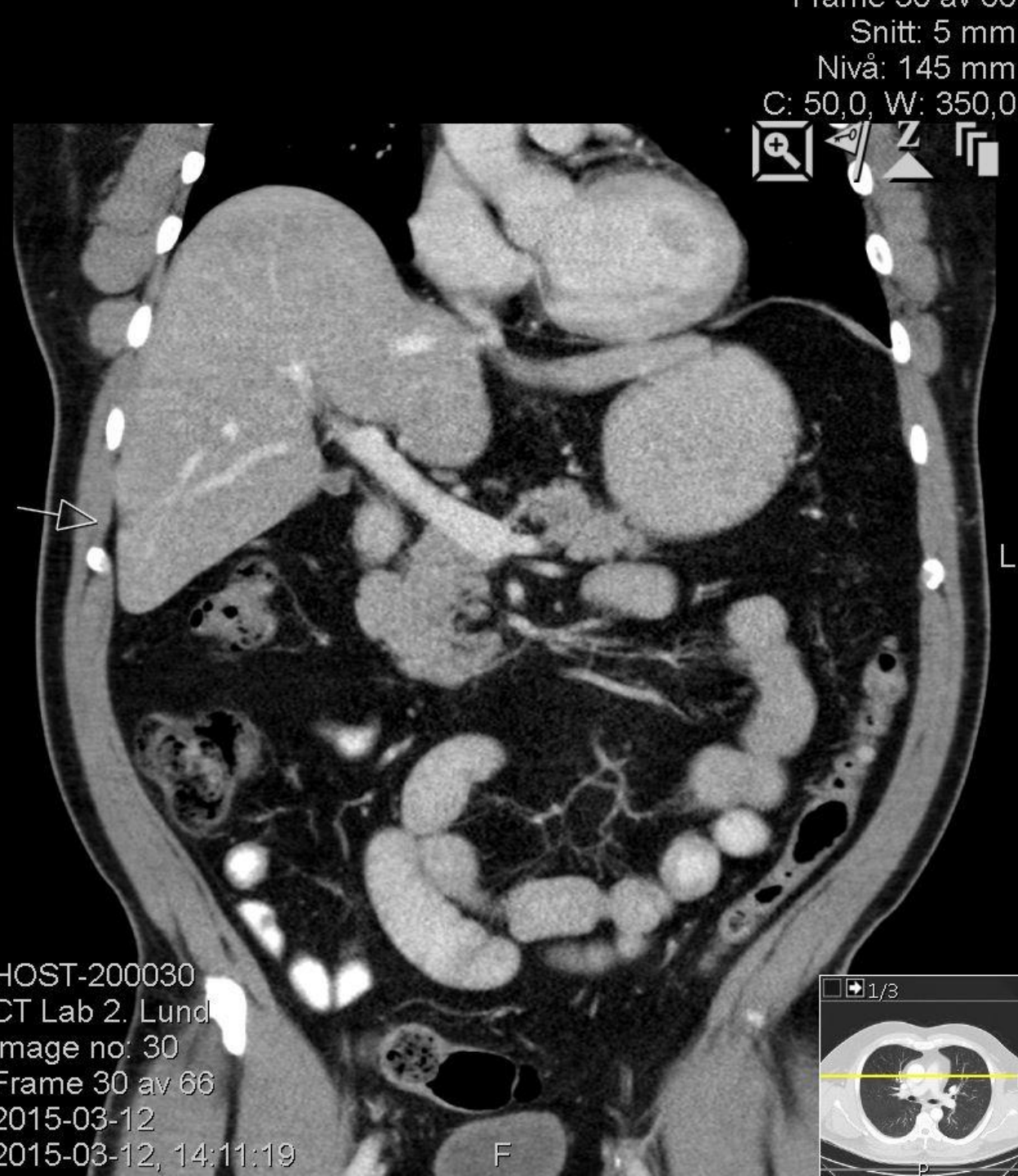
- ▶ Rare entity, < 1% of all sarcomas
- ▶ Two types:
 - a) a usually slow-growing classical or “distal” type starting with cutaneous nodules resulting in skin ulcers; age usually 10 – 40 years
 - b) a more aggressive “proximal” type with deep-seated lesions in the trunk; age usually 20 – 65 years
- ▶ Worse diagnosis:
 - proximal type
 - male gender
 - early metastatic disease

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- ▶ 49 year old man with diabetes and hypertension
 - ▶ In the autumn of 2014 he got a growing ulcerous tumour on his scalp
 - ▶ Surgical excision showed an epithelial sarcoma
 - ▶ Somewhat later, several smaller cutaneous nodules appeared on the scalp and biopsy verified the same type of tumour
 - ▶ CT scan showed a 3 cm large tumour in the right lung and a suspected growth in right liver lobe
 - ▶ Biopsy of the lung lesion verified epithelial sarcoma



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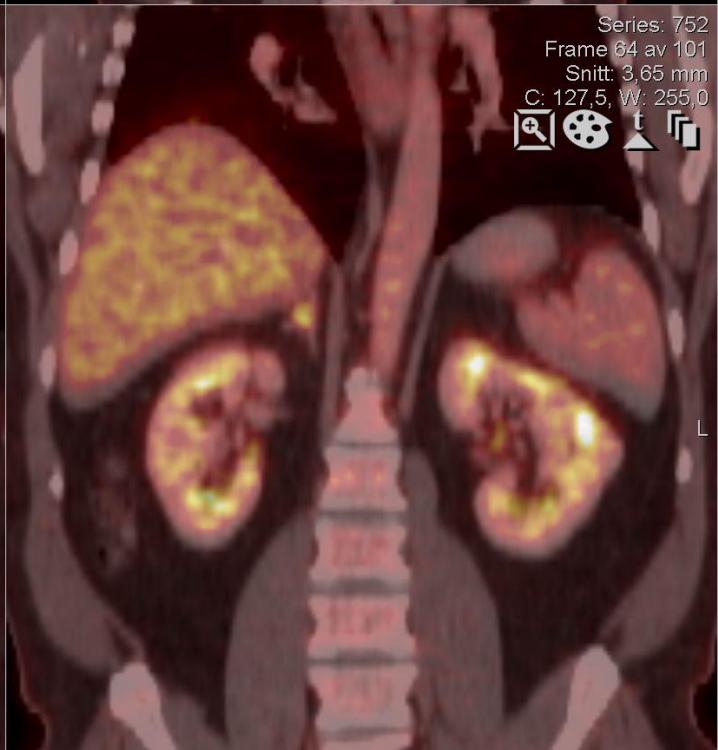
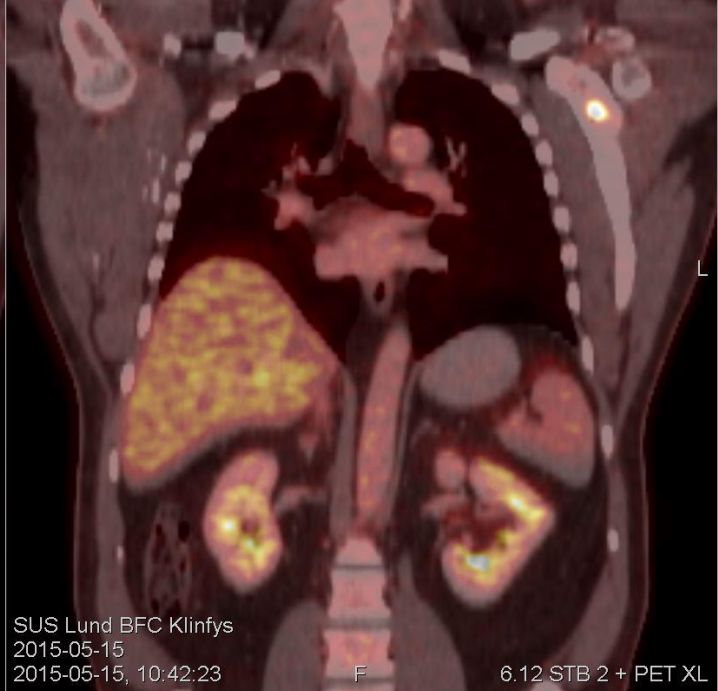
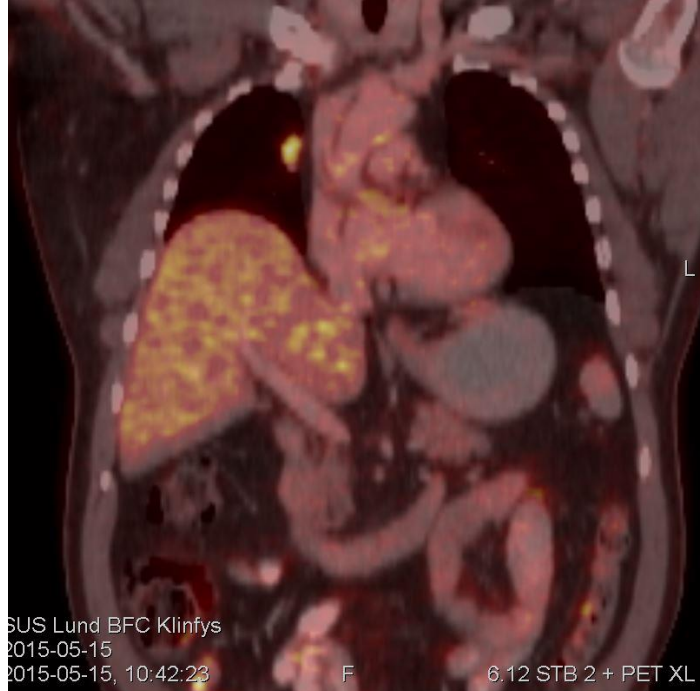



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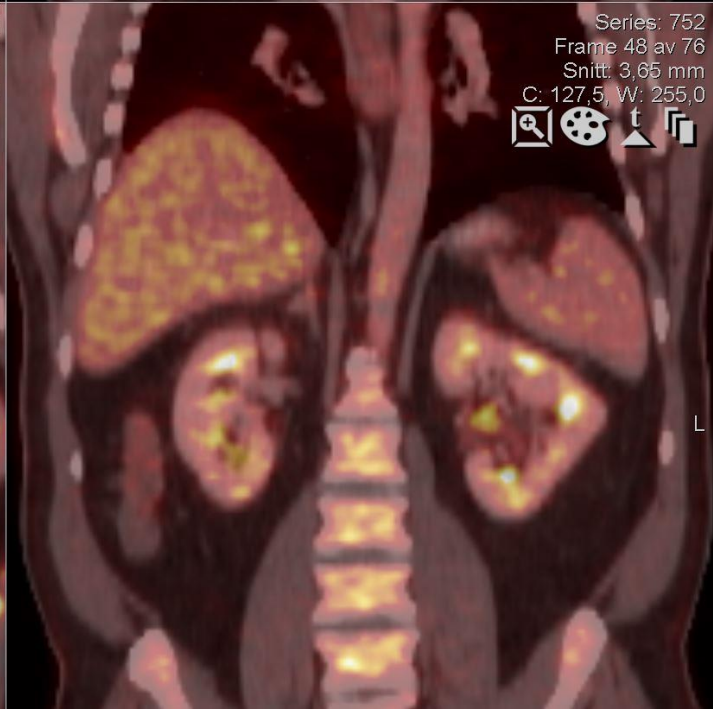
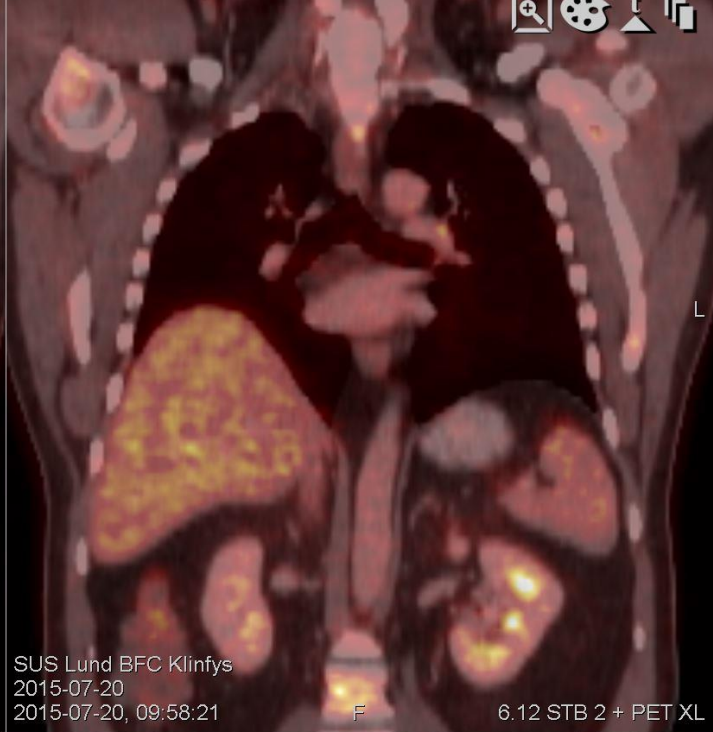
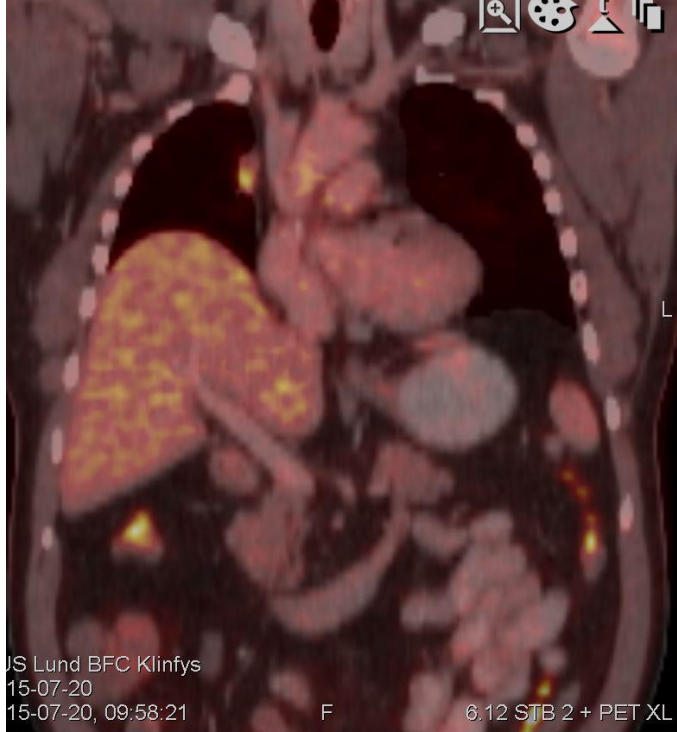
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- Referred for chemotherapy
 - Before start, a PET-CT was performed showing highly suspected metastases in
 - right lung
 - right liver lobe
 - right adrenal gland
 - left scapula



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- Based on earlier experience in epithelial sarcoma, gemcitabine may be a drug of choice
 - Started on gemcitabine-docetaxel
 - Because of skeletal involvement (scapula) he also started denosumab
 - After first cycle of chemotherapy small nodules at the scalp decreased in size, and pain in the left shoulder became less severe
 - Evaluation with new PET-CT after 3 cycles showed metabolic regression except for lung, but decreased size in the lung



C: -4,0, W: 506,9




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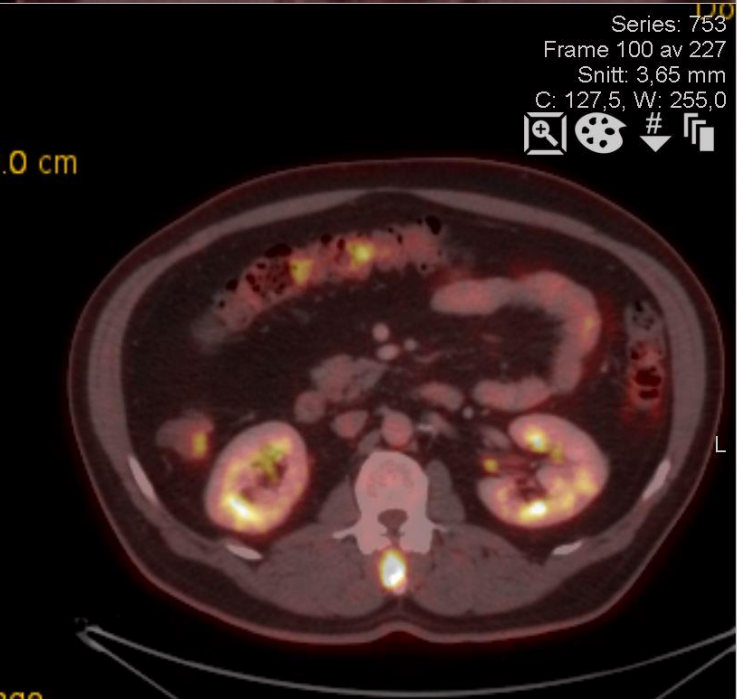
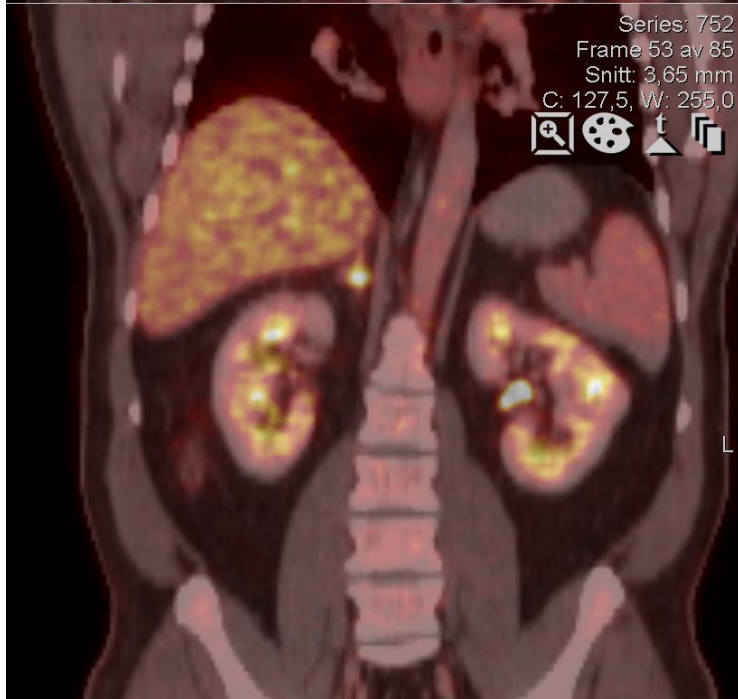
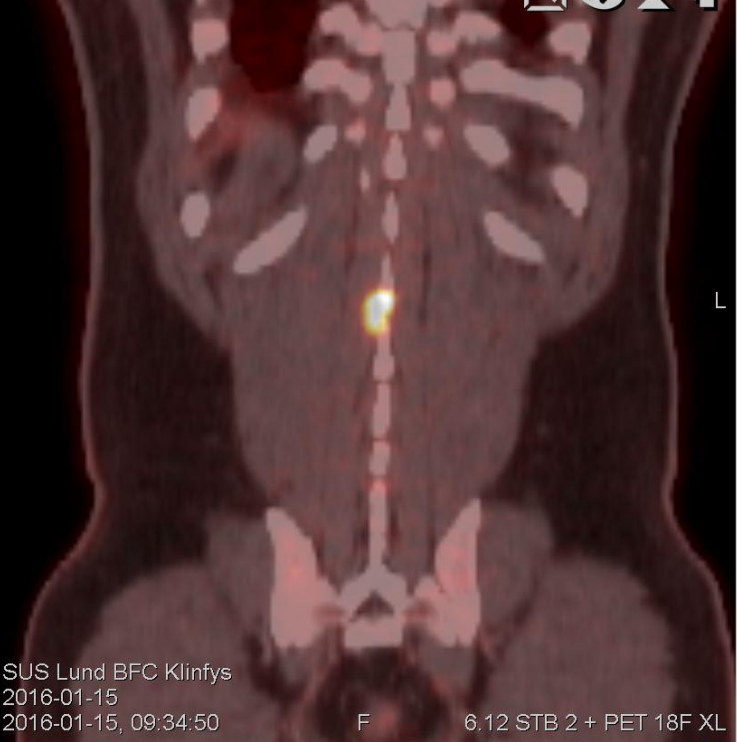
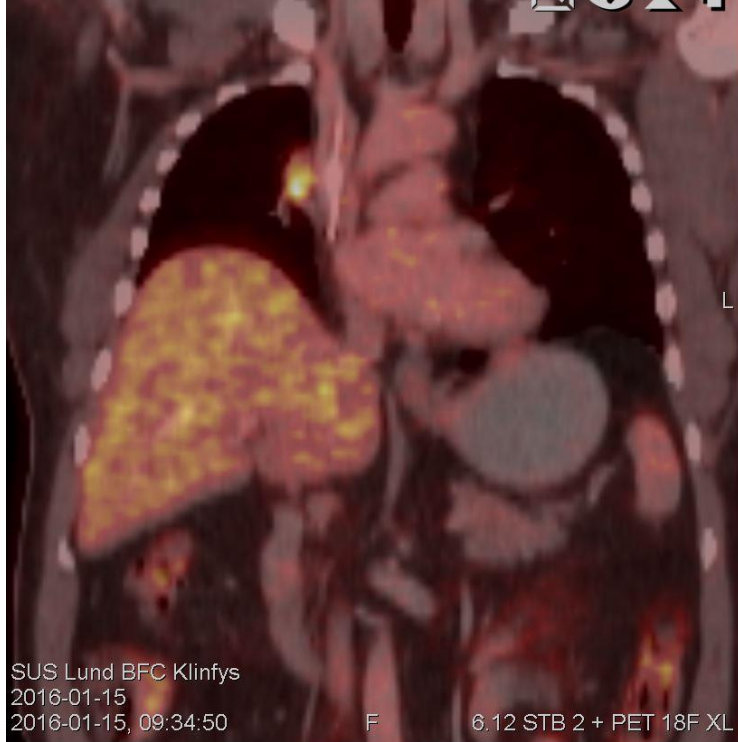
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- ▶ Continued with gemcitabine – docetaxel, but increasing neuropathy made us lower docetaxel dose in cycle 4 and after that no more docetaxel was given
 - ▶ Received single gemcitabine x 5
 - ▶ Tolerated treatment well and a new PET-CT in September showed slight further metabolic regression



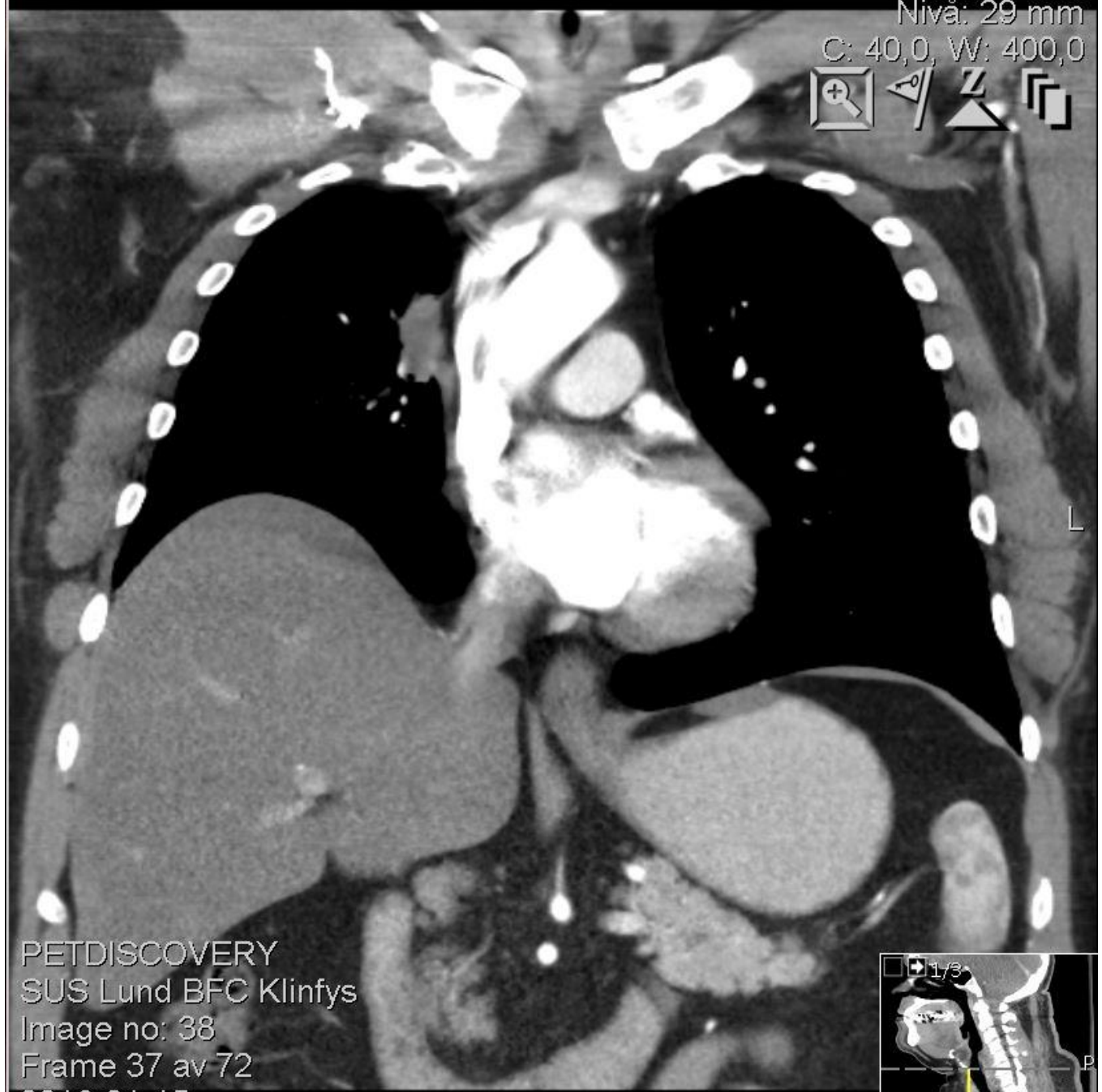
► What to do now?

- go on with gemcitabine until progression?
- switch to something else?
- treatment pause?

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- We agreed with the patient to have a pause in treatment a couple of months and then perform a new evaluation
 - A new PET-CT seven weeks after last gemcitabine cycle showed progressive disease in the lung, thoracic wall, right adrenal gland and lumbar spine



Nivå: 29 mm
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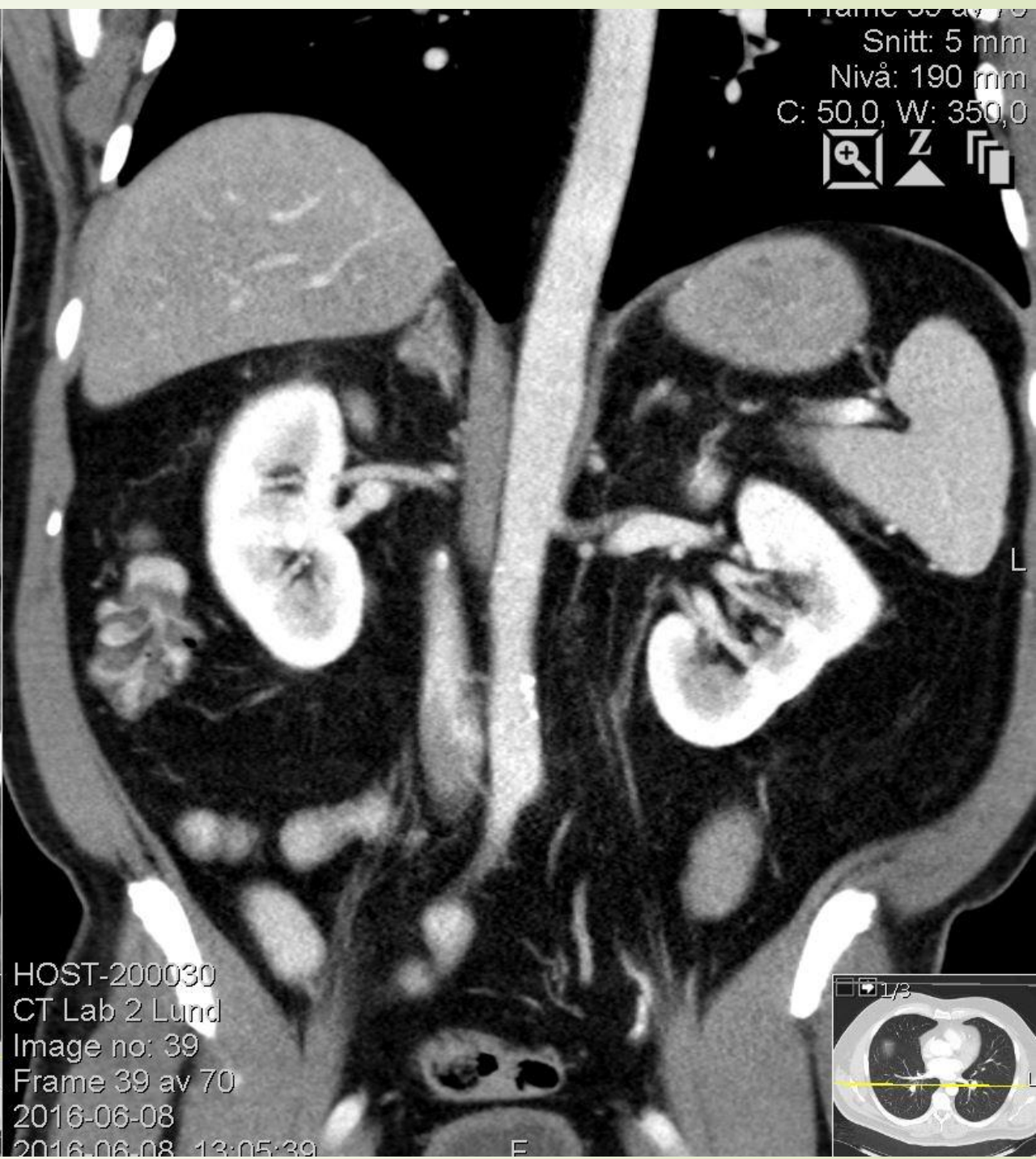
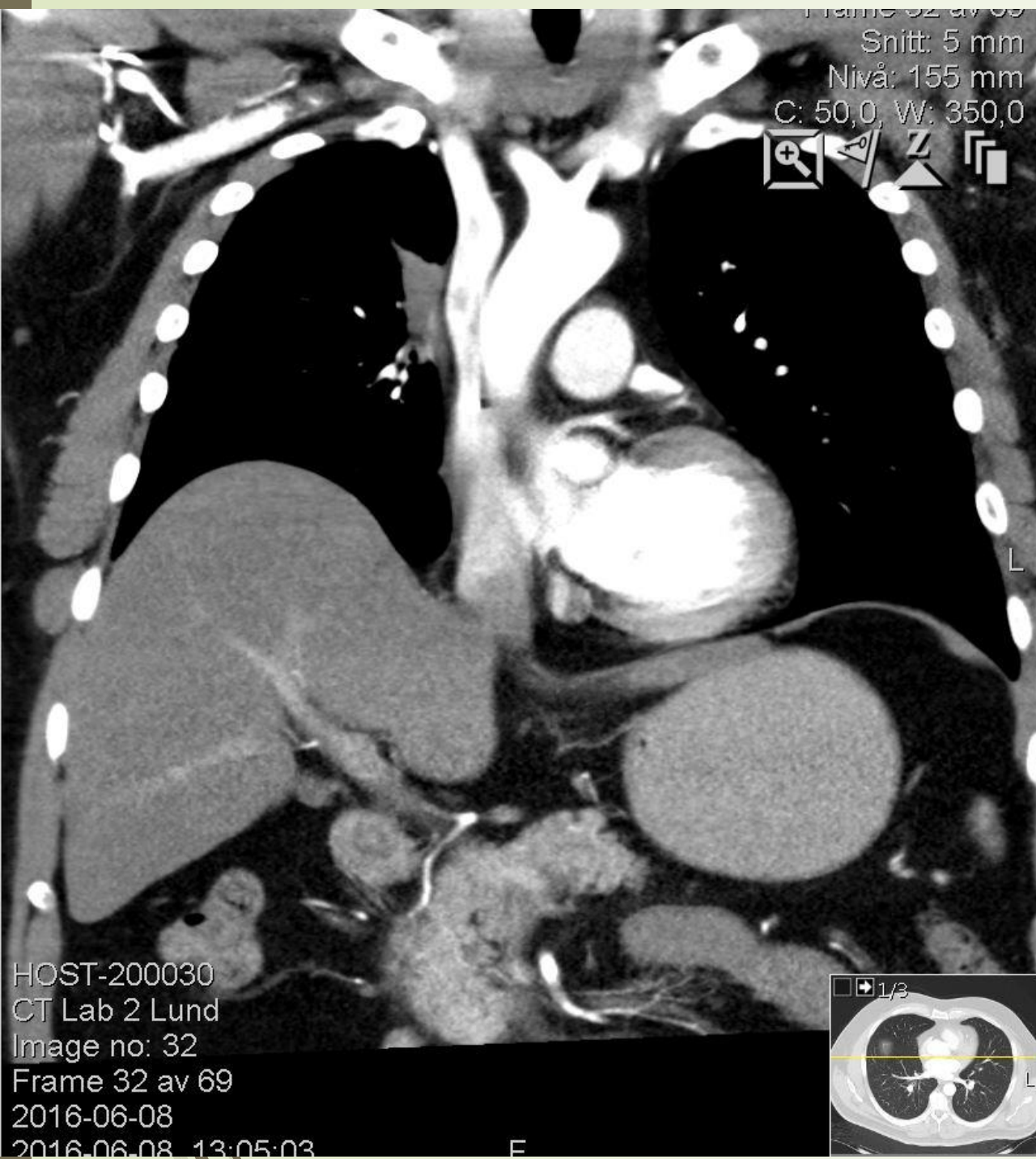
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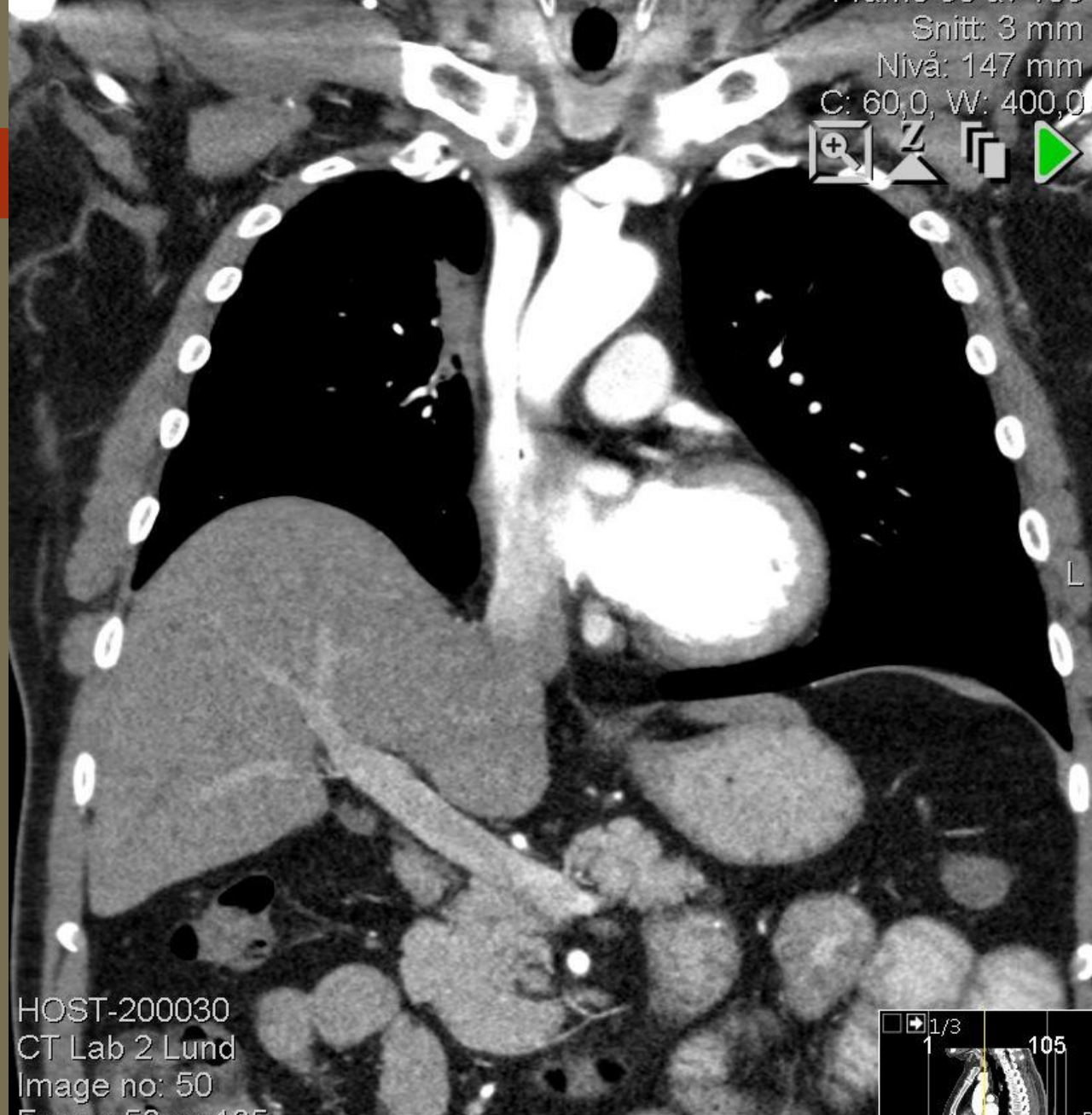


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- Thus, short-lasting effect of gemcitabine-based therapy
 - We considered to start gemcitabine again, but also informed the patient about the ANNOUNCE trial where he was eligible
 - Wanted to join the trial with doxorubicin combined with olaratumab or placebo
 - He obviously did not get placebo since he had a severe infusion-related skin toxicity with massive urticarial toxicodermia
 - Had to stop olaratumab
 - What to do now?
 - continue doxorubicin single?
 - some other treatment?

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- ▶ We considered doxorubicin, and also to go back to gemcitabine
 - ▶ However, based on case reports and own good experiences we decided to suggest the patient a shift to TKI treatment
 - ▶ Votrient (pazopanib) was started in early April 2016
 - ▶ Tolerated treatment well, some fatigue but continued to work halftime
 - ▶ First evaluation with PET-CT was done in June → clear regression in the lung and slight in the adrenal gland

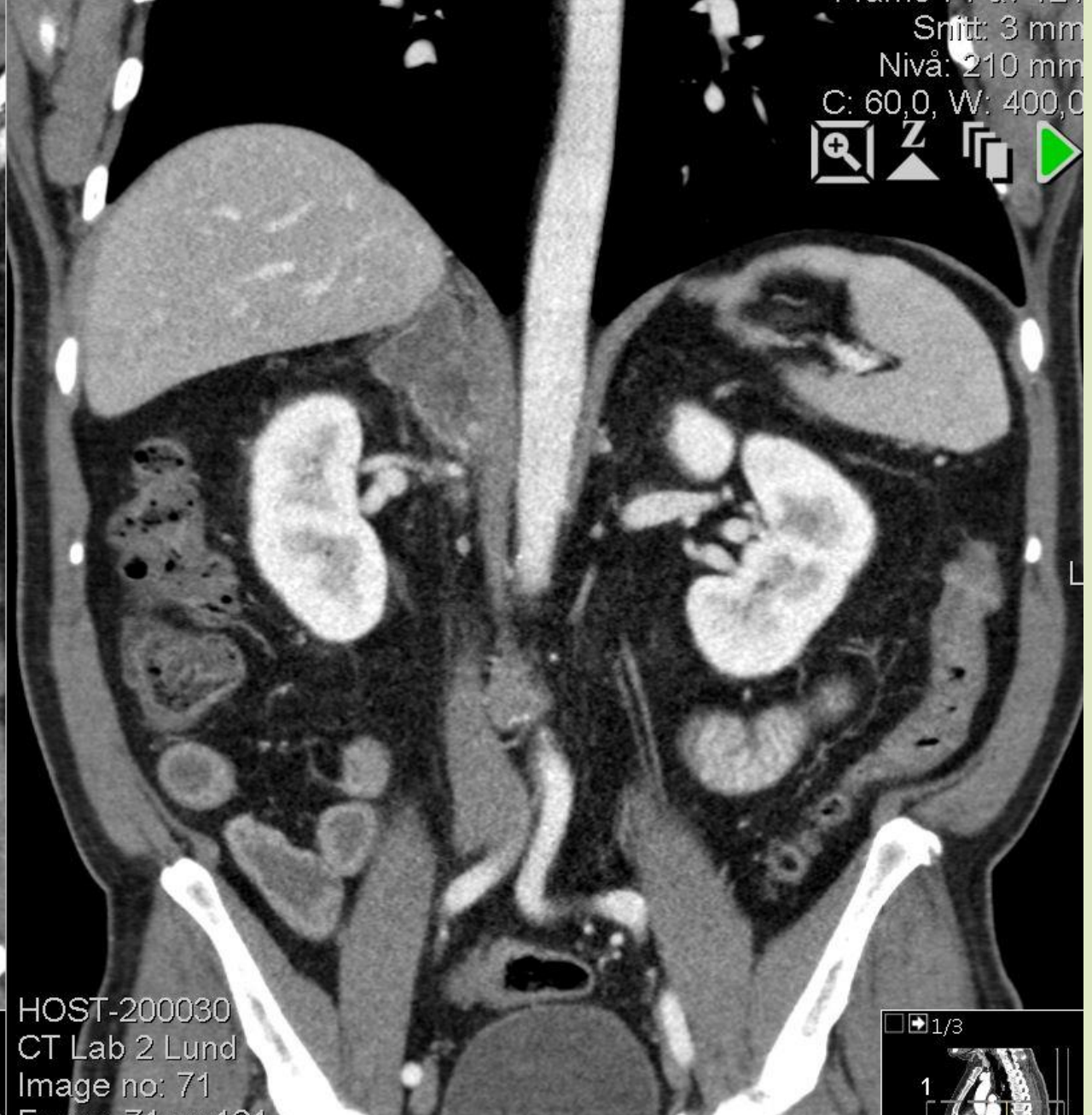
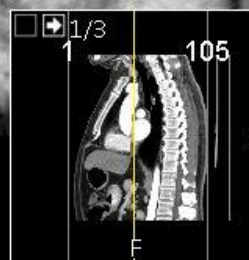


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- ▶ Continued Votrient and is still on this treatment after almost 3 years
 - ▶ Some increase in side effects with diarrhoea and joint pain → dose has been decreased from 800 to 600 and later 400 mg; good tolerance on this dose
 - ▶ Stable disease in lung, liver and scapula but slow progression over time in right adrenal gland
 - ▶ No disease related symptoms
 - ▶ CT scan now usually twice yearly, last time in late June 2018



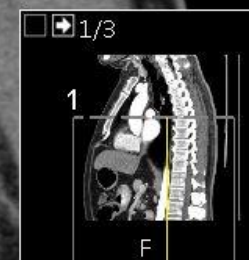
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- ▶ The treatment thus well tolerated on decreased dose of Votrient and the sarcoma is under control except for a growing metastasis in the adrenal gland – what to do about that?
 - nothing since there are no symptoms?
 - increase the Votrient dose?
 - change to other treatment, and if so, which one?
 - surgical removal of the adrenal gland and continue with Votrient?
 - radiotherapy instead of surgery?



Lessons from this case

- ▶ Epithelioid sarcoma may respond at different types of therapy
 - ▶ Prognosis may be rather good even with internal organ involvement
 - ▶ Pazopanib may have long-time effects in some cases of sarcoma
 - ▶ Mixed response do not seldom occur in sarcoma treatment
 - ▶ Medical treatment may sometimes need to be combined with local methods
- 