Spondylodiscitis

Aetiology, diagnostics, therapy

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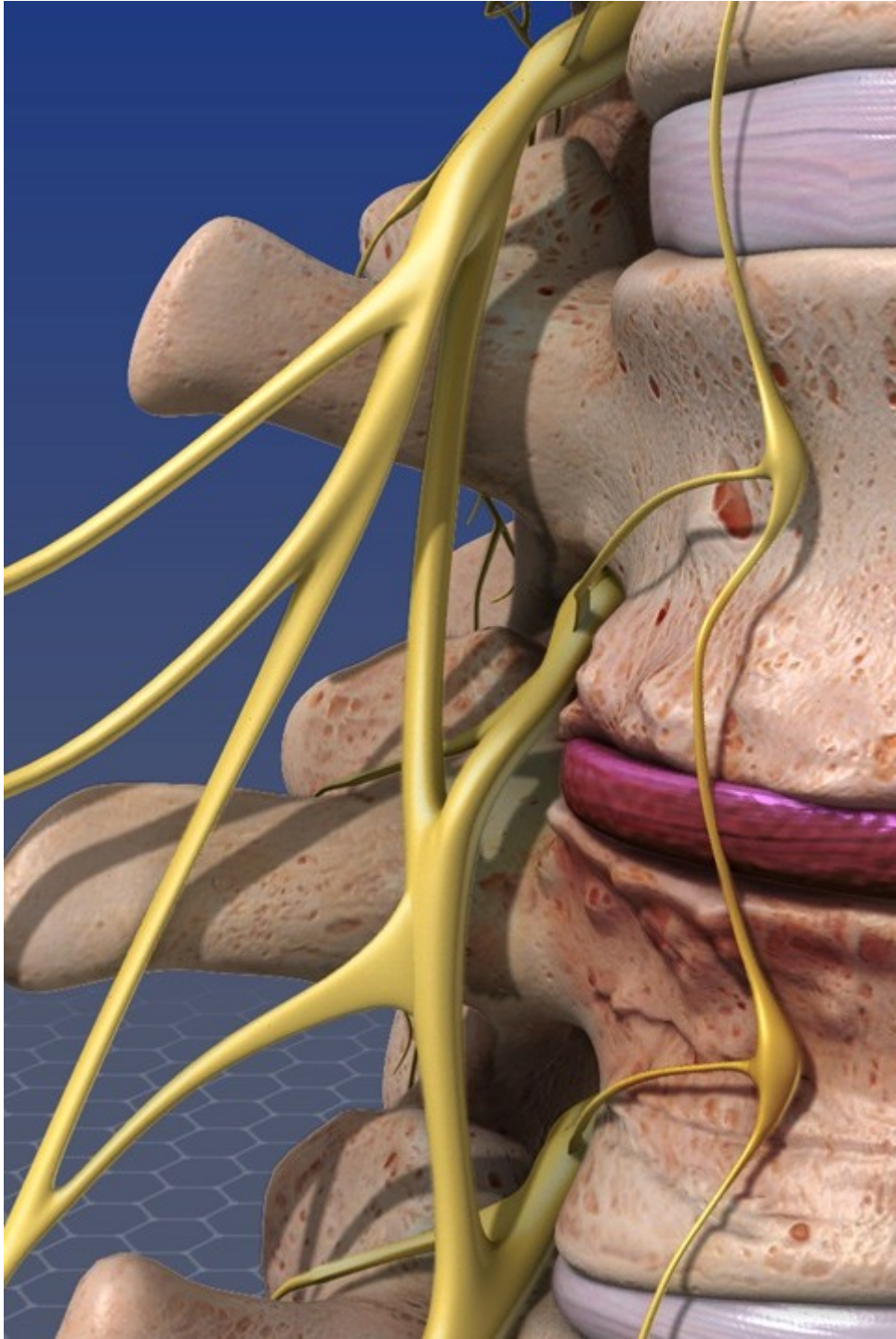
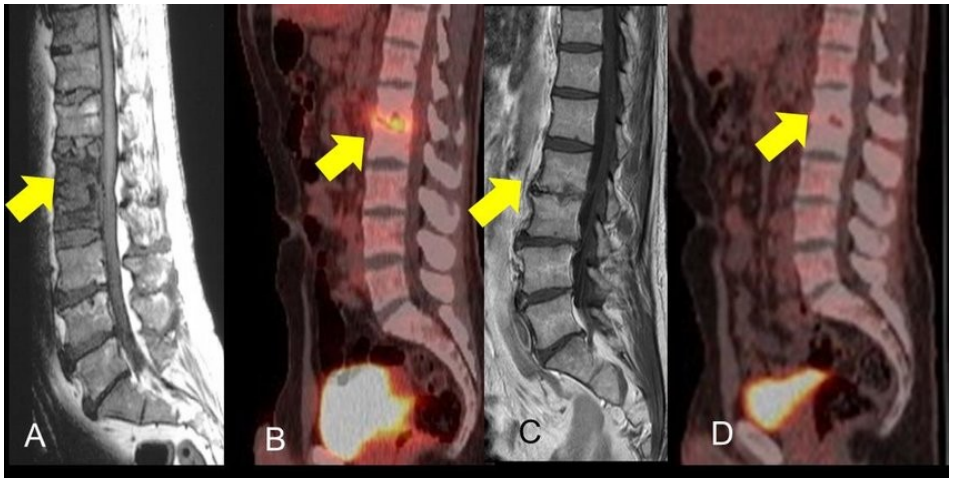


MOTTO

“Discitis from the infectologist’s and orthopaedist’s point of view”

“Multidisciplinary issue = multidisciplinary approach”



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Společnost infekčního lékařství *ČLS JEP*

FAKULTNÍ NEMOCNICE BRNO

MUNI MED

PRESENTATION PLAN

- Definition
- Epidemiology
- Aetiopathogenesis
- Clinical symptoms
- Diagnostics
- Imaging methods
- Treatment

- Case studies
- Discussion

Definition

Various infections of the spine and adjacent structures, incl. soft tissues

It includes discitis, epidural abscess and vertebral osteomyelitis

MRI scans of the spine are the foundation of diagnostics

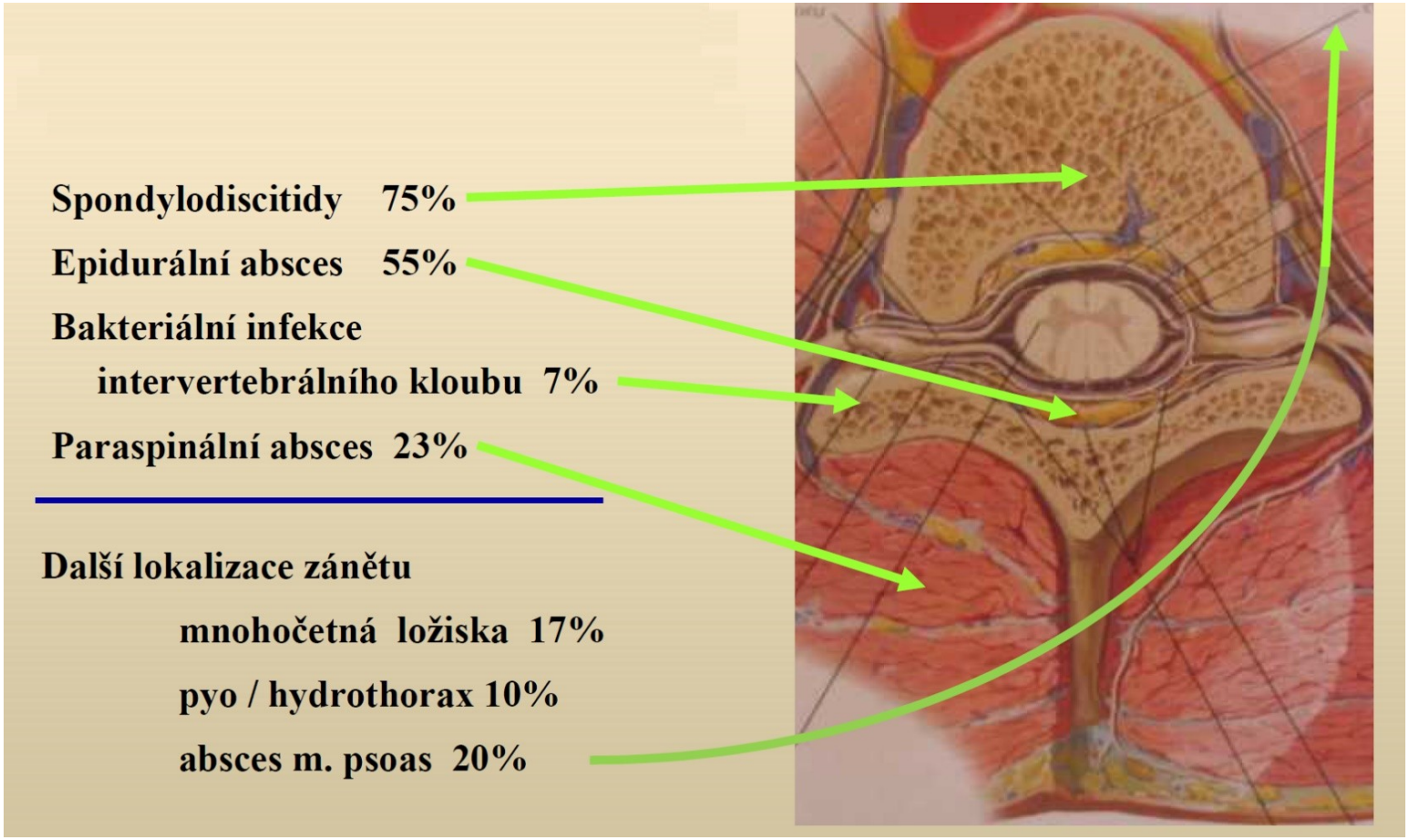
Treatment can be:

- Conservative = long-term targeted antibiotics
- Surgical = decompression, possible stabilisation of the spine and long-term ATB

The approach is always individual, and depends particularly on:

- The patient's general condition
- The extent and chronicity of the infection
- The inflammation’s localisation in the spine
- Identification of the pathogen and its susceptibility to antimicrobial agents

Anatomy – the localisation of the inflammatory process



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Epidemiology I

Incidence range **0.2– 3.7/ 100,000 per year**

3– 5% of all bone and joint infections, **rising incidence**

Bi-modal age distribution:
First peak **under 20 years**
Second peak **50 to 70 years**

Males affected more frequently than females (1.5–2:1 ratio)

30 to 50% associated with **neurological deficit**

Mortality < 5%

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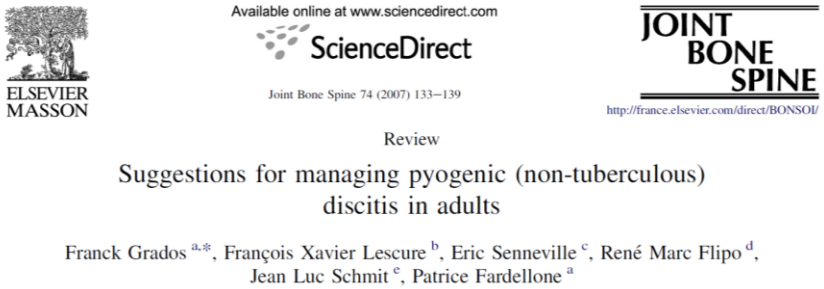
Epidemiology II

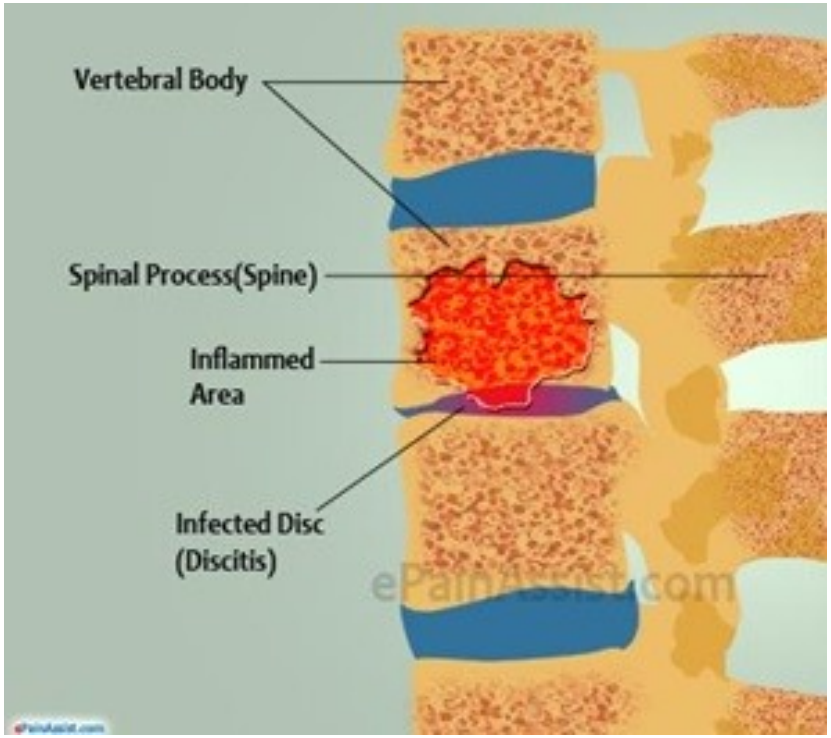
- Anatomical localisation: **50% LS, 40% Th, 10% C spine**

- **Risk factors:**
  - The elderly
  - Type 1 and 2 DM
  - Malignancies
  - Chronic renal failure, liver cirrhosis
  - Chronic cardiac failure, malnutrition
  - Severe obesity
  - HIV infection, alcohol abuse, narcotics
  - Trauma, smoking



Pathogenesis

- Pathophysiology
- Pathogenic microbes
- Inoculation – hematogenic – iatrogenic – per continuitatem
- Neurogenic deficit
- Other complications



Pathogens

- Aetiology is usually **monobacterial**, successfully identified **only in ca two thirds of cases!**

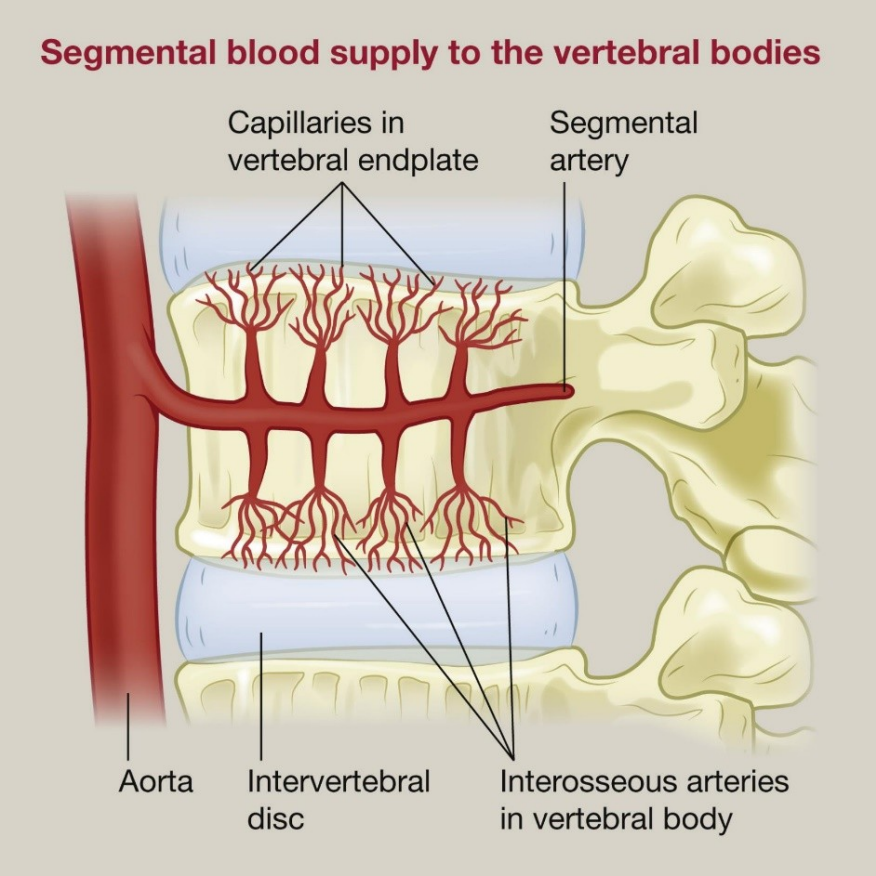
- ***Staphylococcus aureus*** (ca 50% of discitis cases), including **MRSA strains**
- **Enterobacteria** (*E. coli*, *Proteus*, *Klebsiella*, *Enterobacter*...), incl. **ESBL+**

- *Mycobacterium tuberculosis* (specific aetiology, developing countries)
- **Brucellosis** (*B. melitensis*, *B. abortus*, **the Mediterranean**, Middle East)
- Mycotic (in immunocompromised patients, ca 2%)

The diagnosis and management of discitis and spinal infection

David A Samy
Surya Gandham
Marcus DeMatas

Pathogenesis

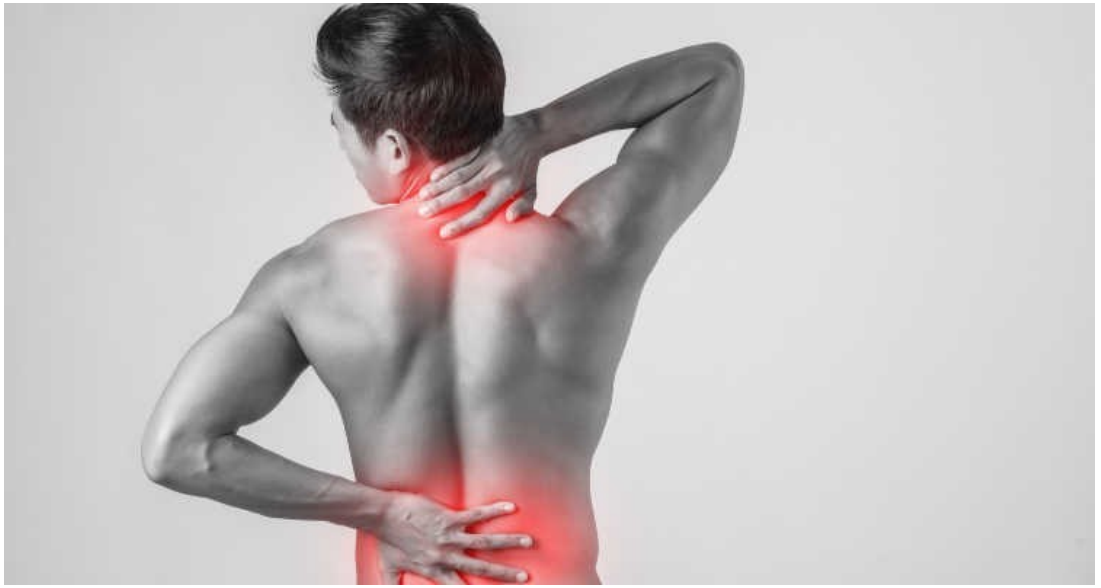


1) The terminal vessels of spinal arteries end in vertebral bodies → **septic emboli cause extensive bone infarctions** → bone tissue defects, **compressive fractures** → **instability of the spine, spread of infection to adjacent discs** → destruction

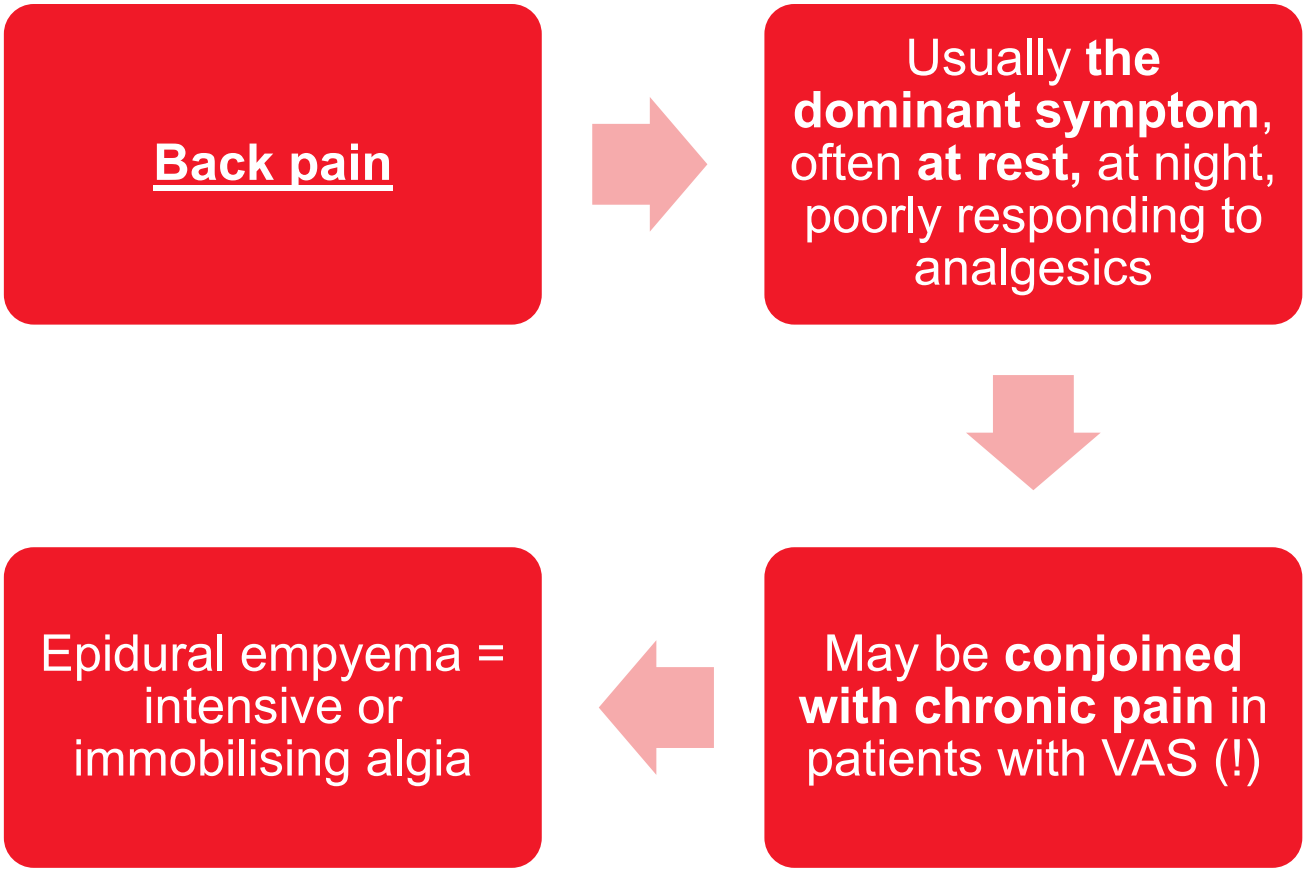
2) The infection spreads from the osteonecrotic lesions further into **the paravertebral soft tissues and the epidural space** of the spinal canal → **abscesses, epidural empyema**

Clinical symptoms

- Back pain
- General symptoms
- Neurological symptoms
- Laboratory markers



Clinical symptoms



Clinical symptoms

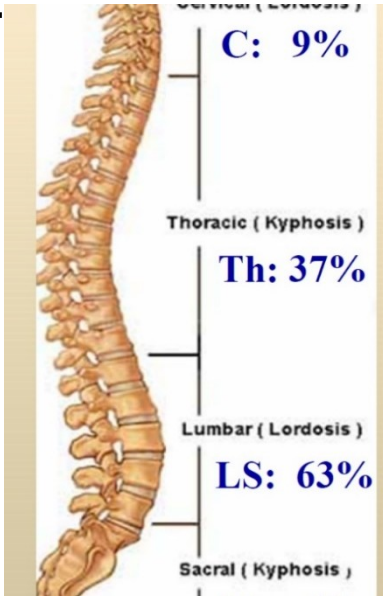
General symptoms of infection

Fever, chills, shivers (rather mild symptoms, septic condition is rare)

Frequent subfebrile temperatures, night sweats, lack of appetite, weight loss, general weakness

Clinical symptoms – neurology

- Radiculopathy, **myelopathy secondary to compression of nerve structures**
- Clinical image ranging from algoparesthesia, paraparesis and paraplegia to **the *cauda equina* syndrome**
- Symptoms depend on the localisation of the inflammatory process:



Odlišná klinika a terapie v závislosti na lokalizaci zánětu!

Skupina 99 pacientů NČB a.s. z let 2014-16

C:	fasciální prostory krku	
	mediastinitida	
	kvadruparéza -plegie	**2%**
Th:	paraparéza / plegie	**20%**
	pyo / hydrothorax	**10%**
LS:	je možné postižení míchy i kaudy (horní L)	
	syndrom kaudy	**8%**
	absces psoatu	**20%**

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Clinical symptoms

Laboratory findings

Elevated **acute phase reactants** (CRP 100–200), **FW typically over 100/min,** low procalcitonin

Leukocytosis, thrombocytosis x thrombocytopenia, **anaemia** (microcytic, protracted course)

Often **rapid CRP decrease (down to normal) after ATB therapy** (FW elevation persists longer!)

CAVE: **“cold infection” (!)**

Diagnostics

Spondylodiscitis is rare, but it does occur!

Persisting **back pain at rest**, often when lying down and at night

"Red flags" febrile and subfebrile temperatures, APR elevation, age below 20 and over 55 years, history of a spinal trauma or surgery, weight loss, fatigue, a new neurological deficit

Spine imaging examination always as soon as possible

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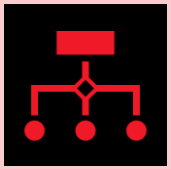
Diagnostics

Imaging methods → key for diagnostics

Microbiology → key for infectious agent determination



Haemocultivation (positive in ca 60% of discitis cases)
Cultivation from a potential lesion (urine, pus...)
Targeted biopsy

Imaging methods

X-ray ⟶ poor sensitivity, vertebral osteomyelitis finding with **2–3 weeks latency**, poor specificity (tumors, pathological fractures...)

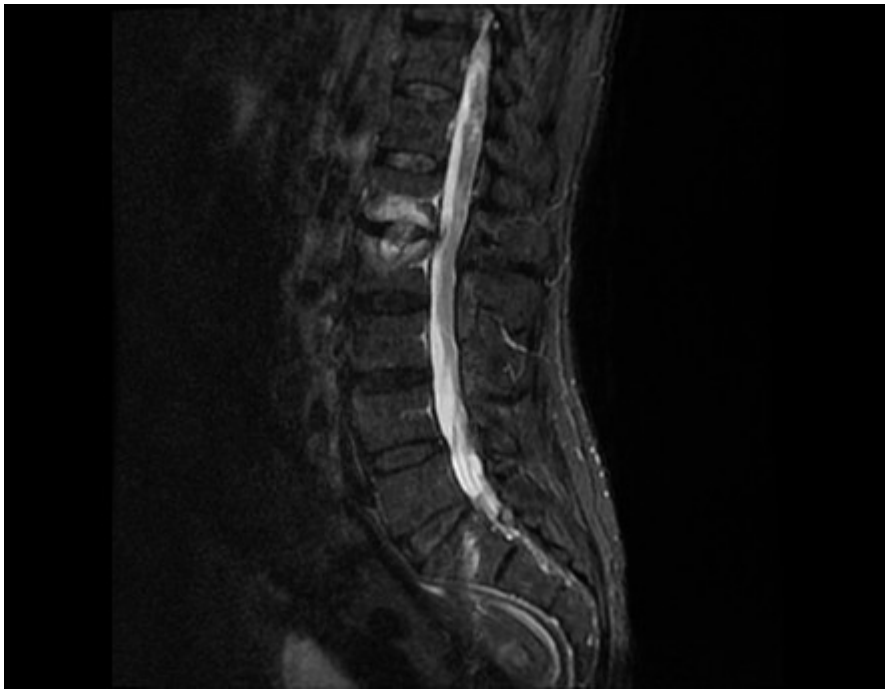
CT ⟶ easier accomplished than MRI, faster, but poorer imaging

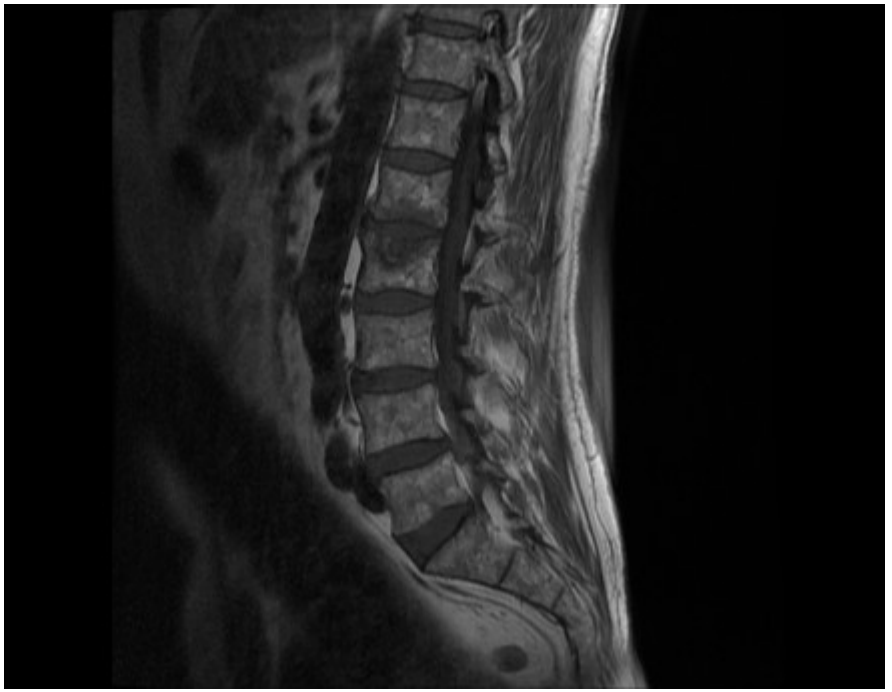
MRI ⟶ gold standard, higher sensitivity and specificity, **captures intervertebral discs**, soft tissues, dg of myelopathy, nerve structures compression

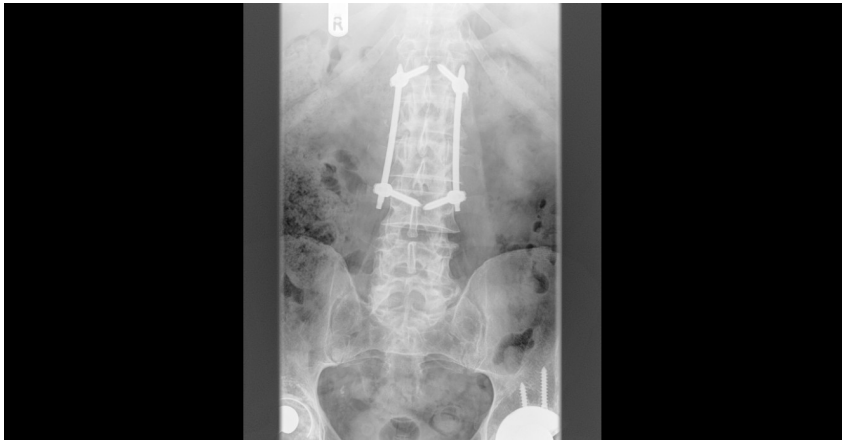
PET/MRI, SPECT/CT ⟶ radionuclide methods, **morphology + functional diagnostics combination**, search for infection origin in FOU, detection of tumors and metastases

Imaging methods

- Simple X-ray image of the spine
- Computed tomography (CT)
- **Magnetic resonance imaging (MRI)**
- Scintigraphy, PET/MRI



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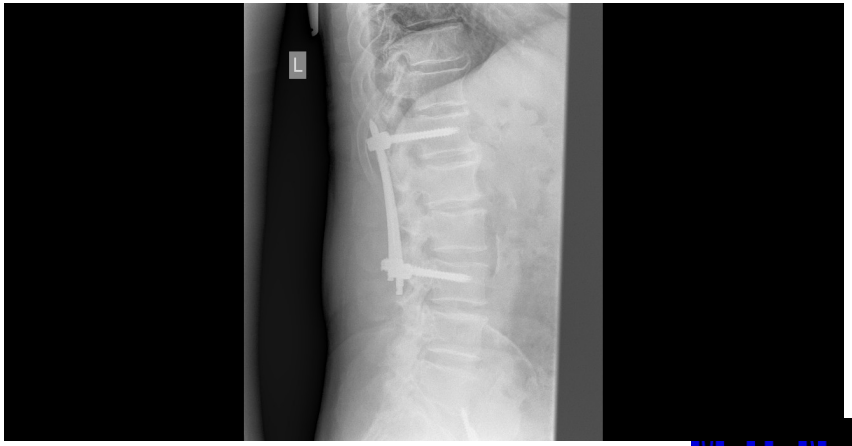
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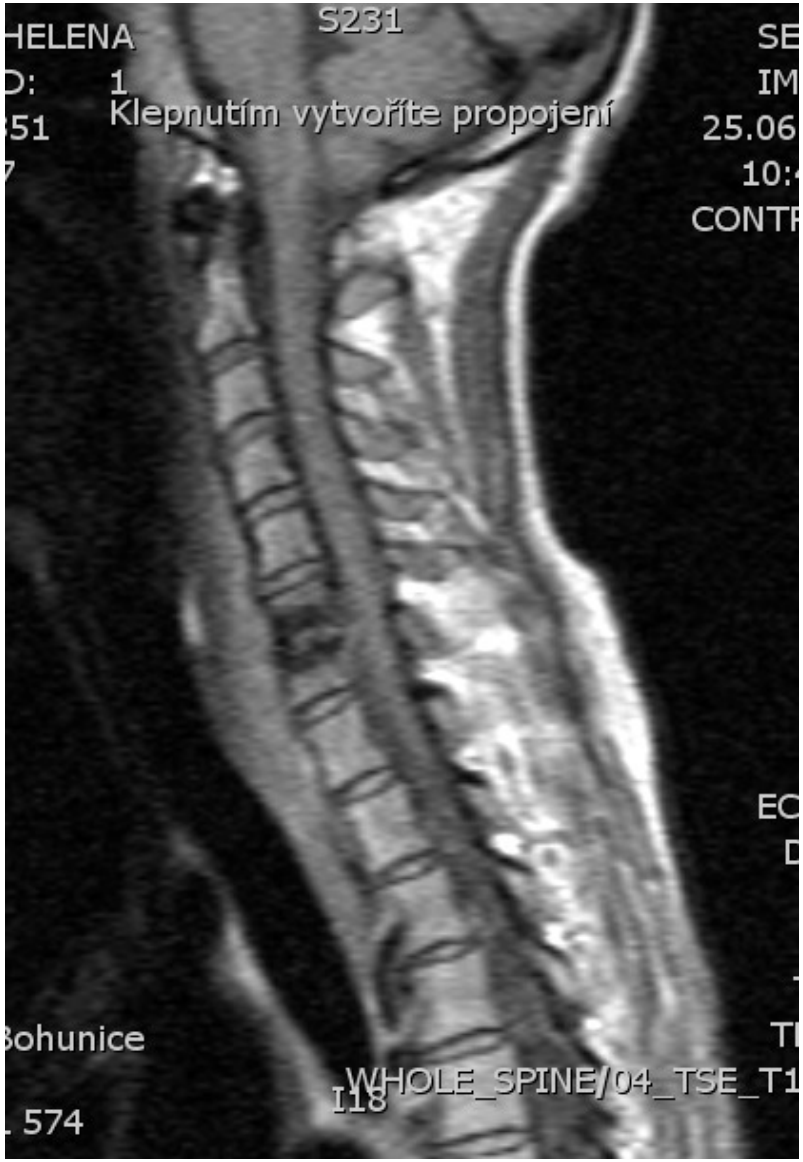
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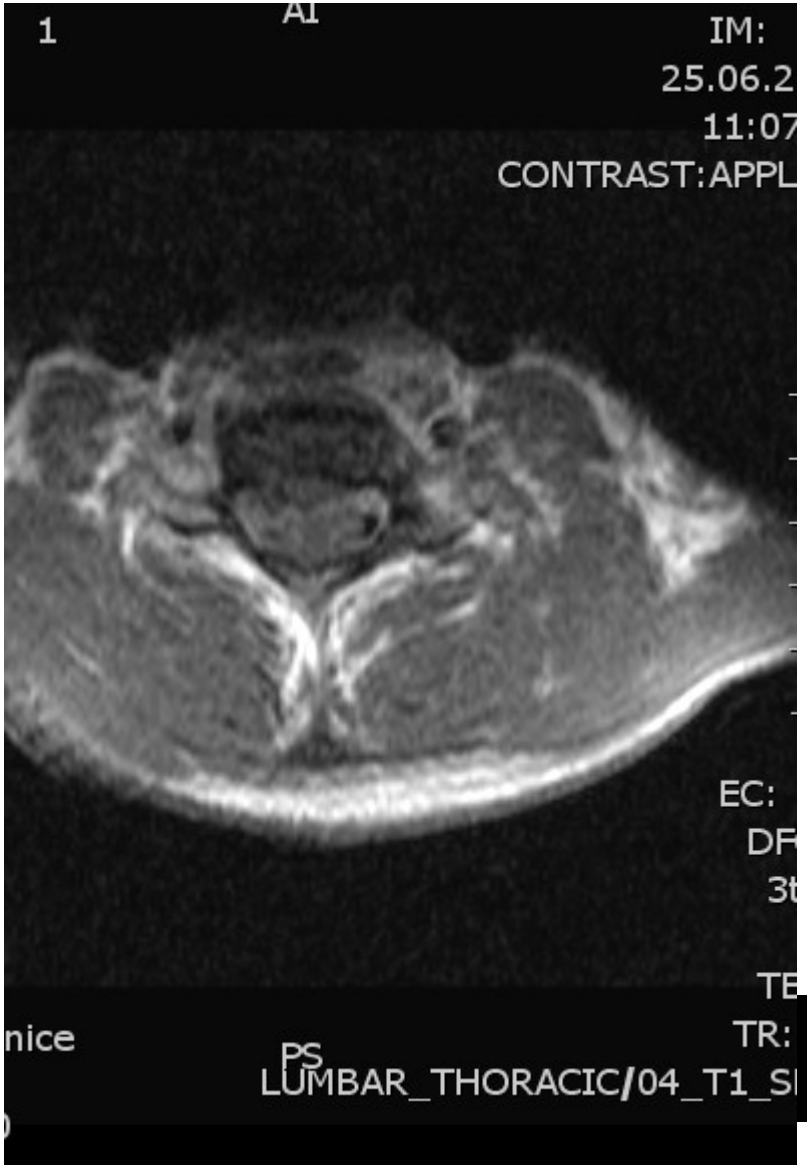
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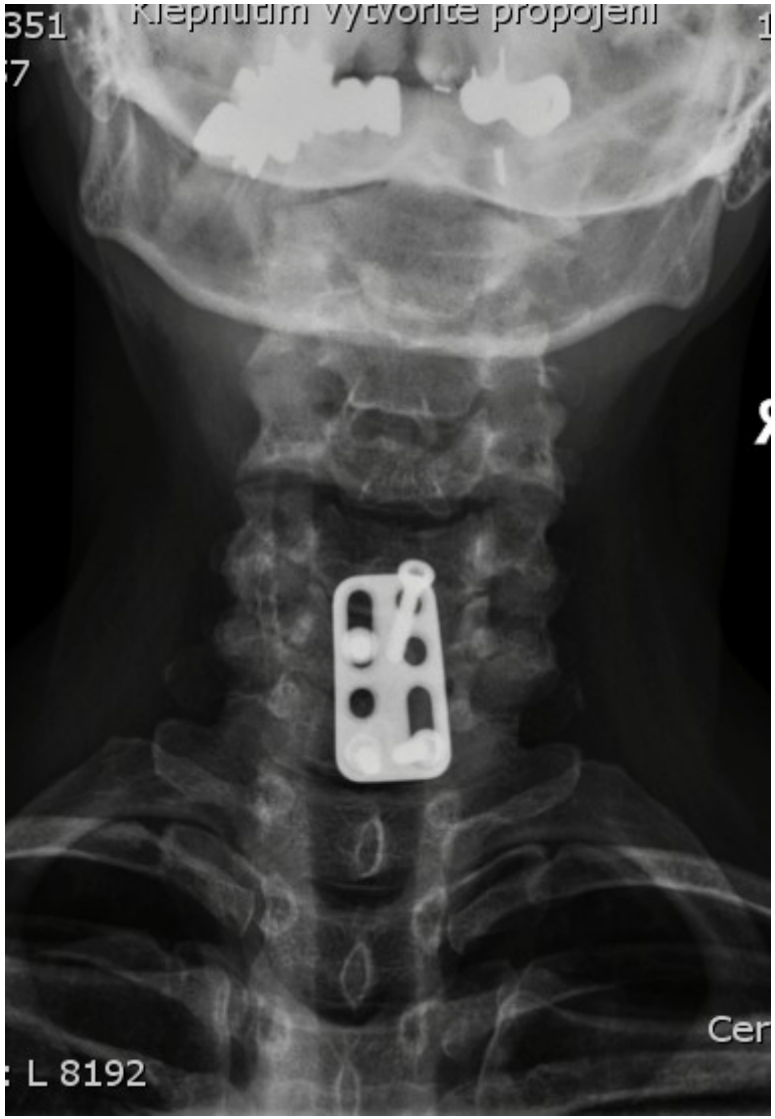
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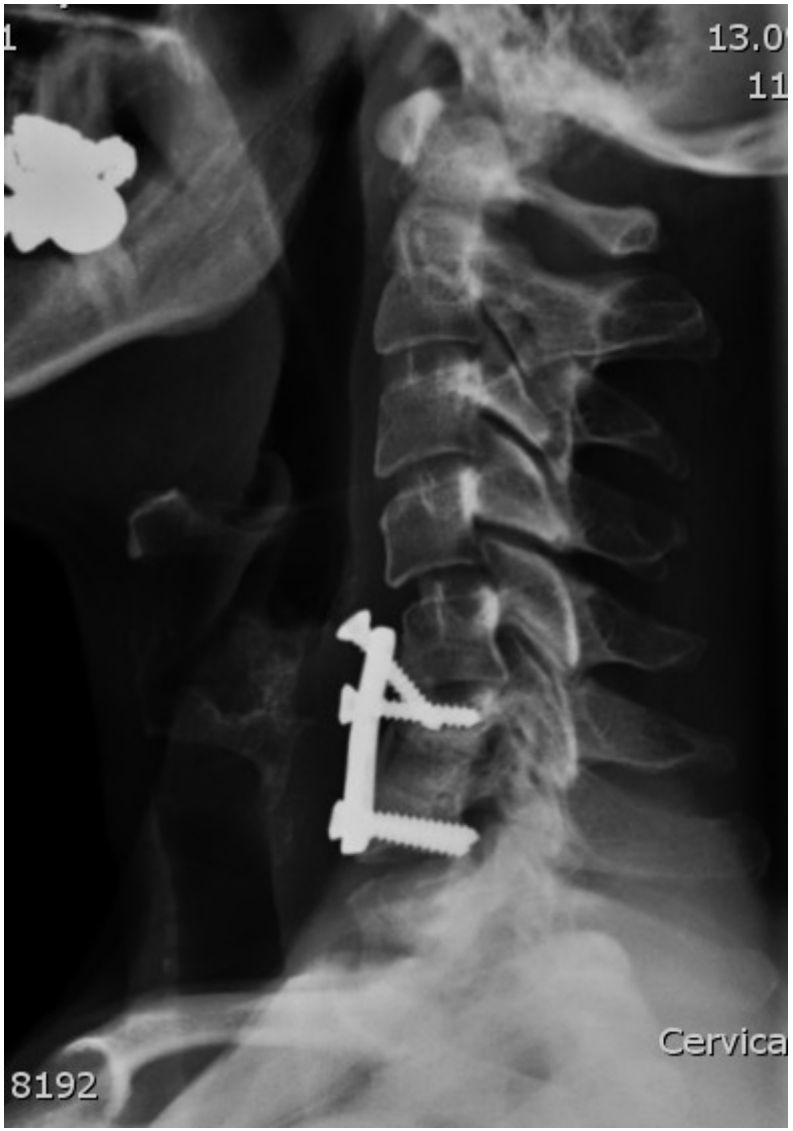
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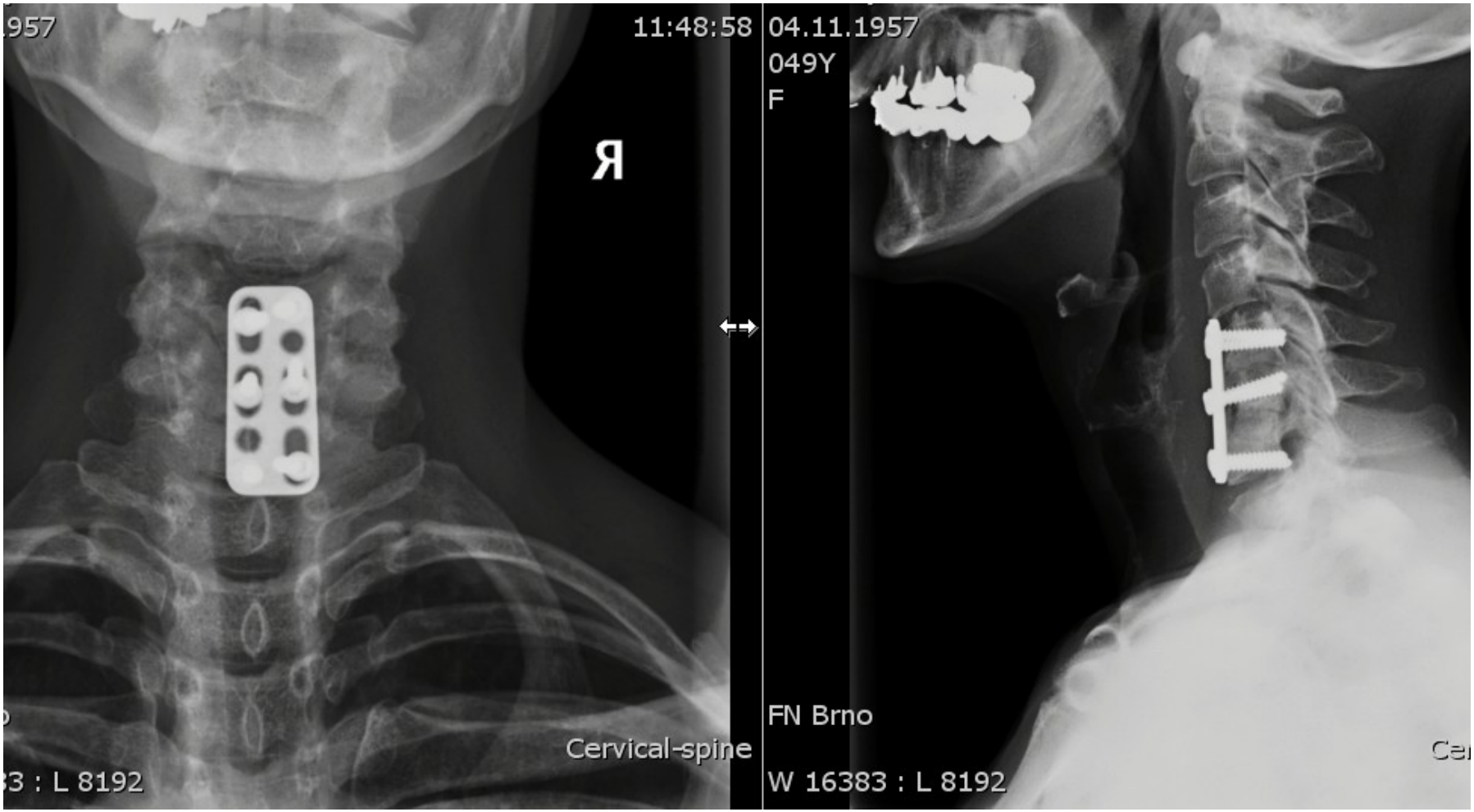
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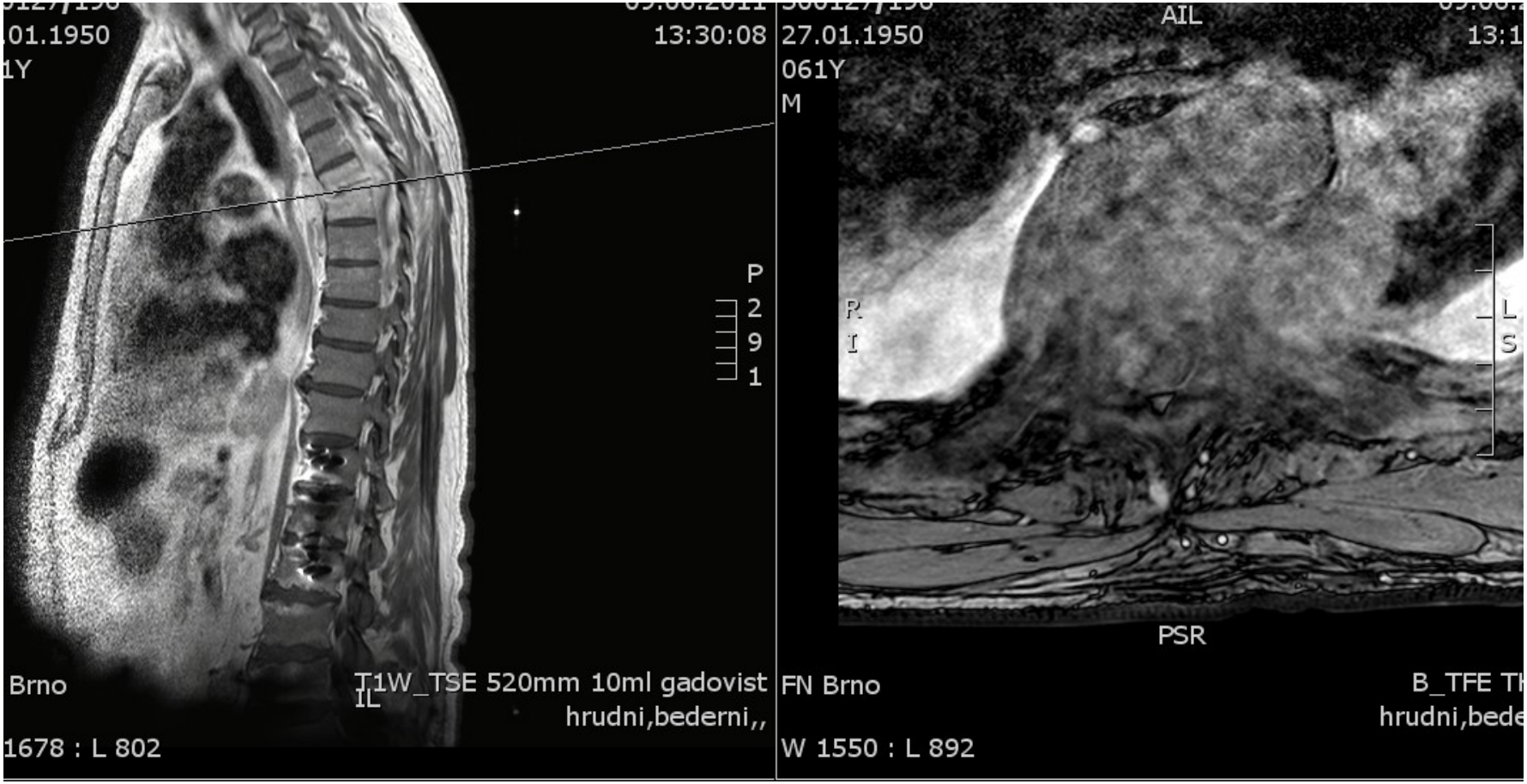
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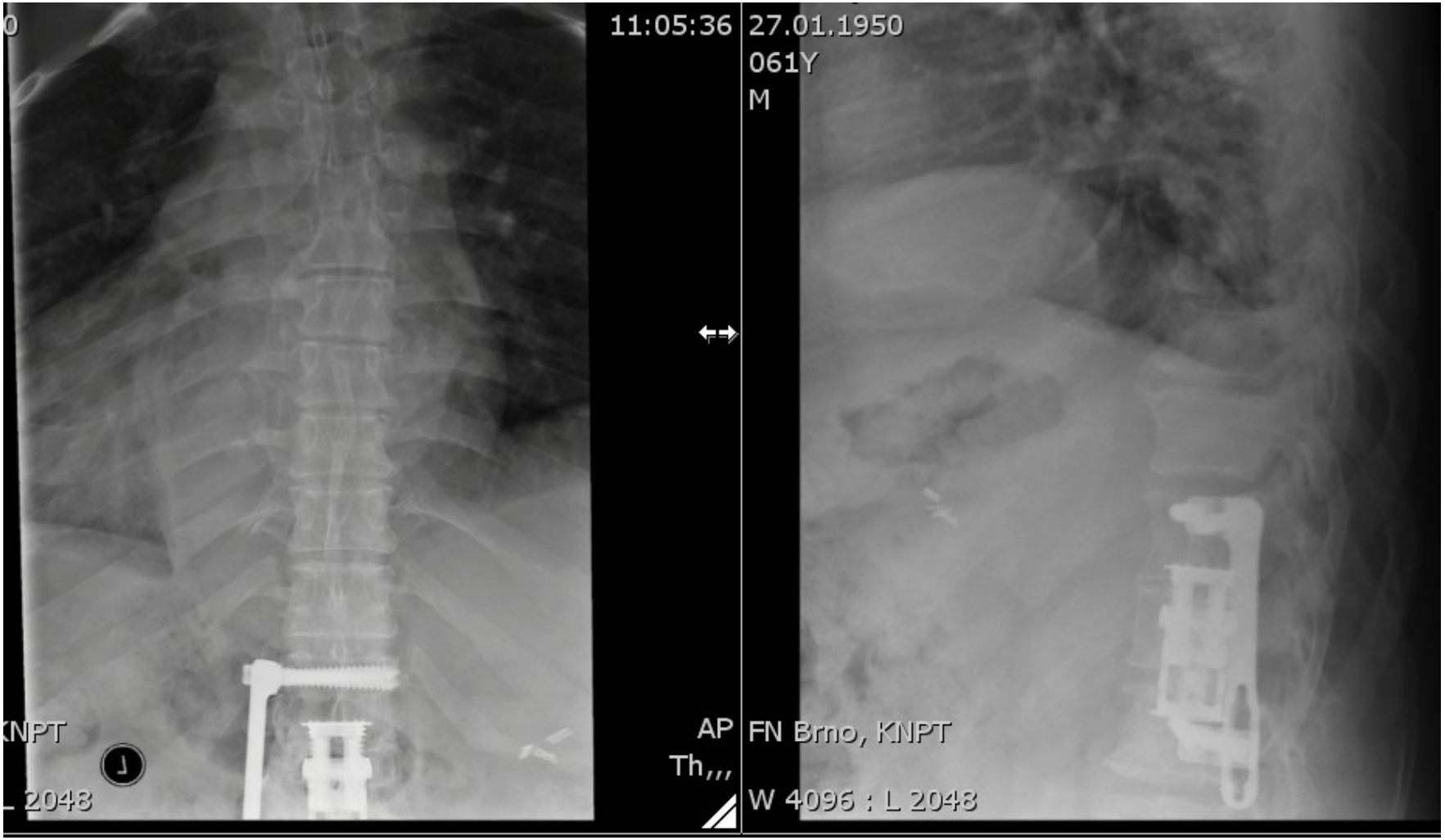
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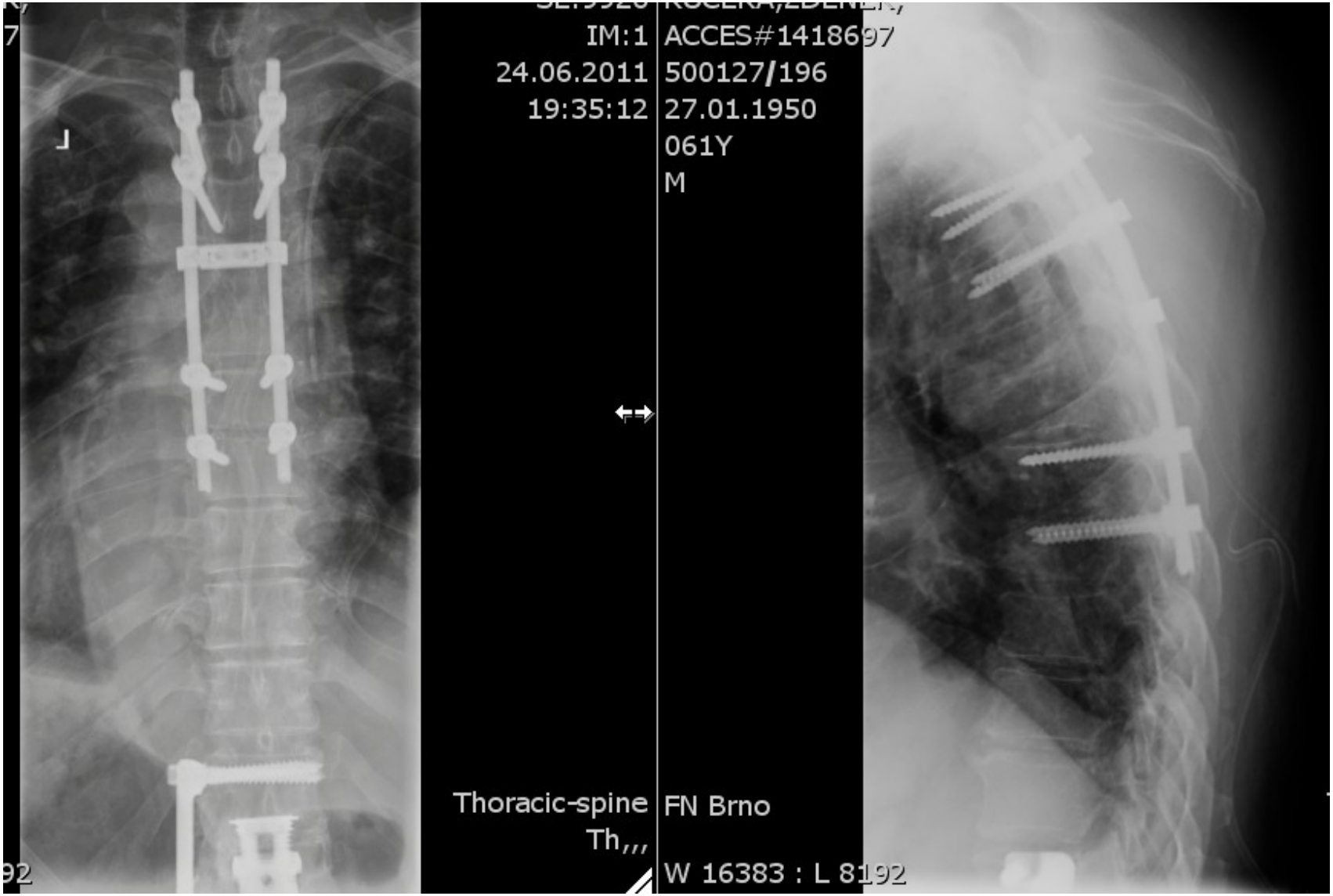
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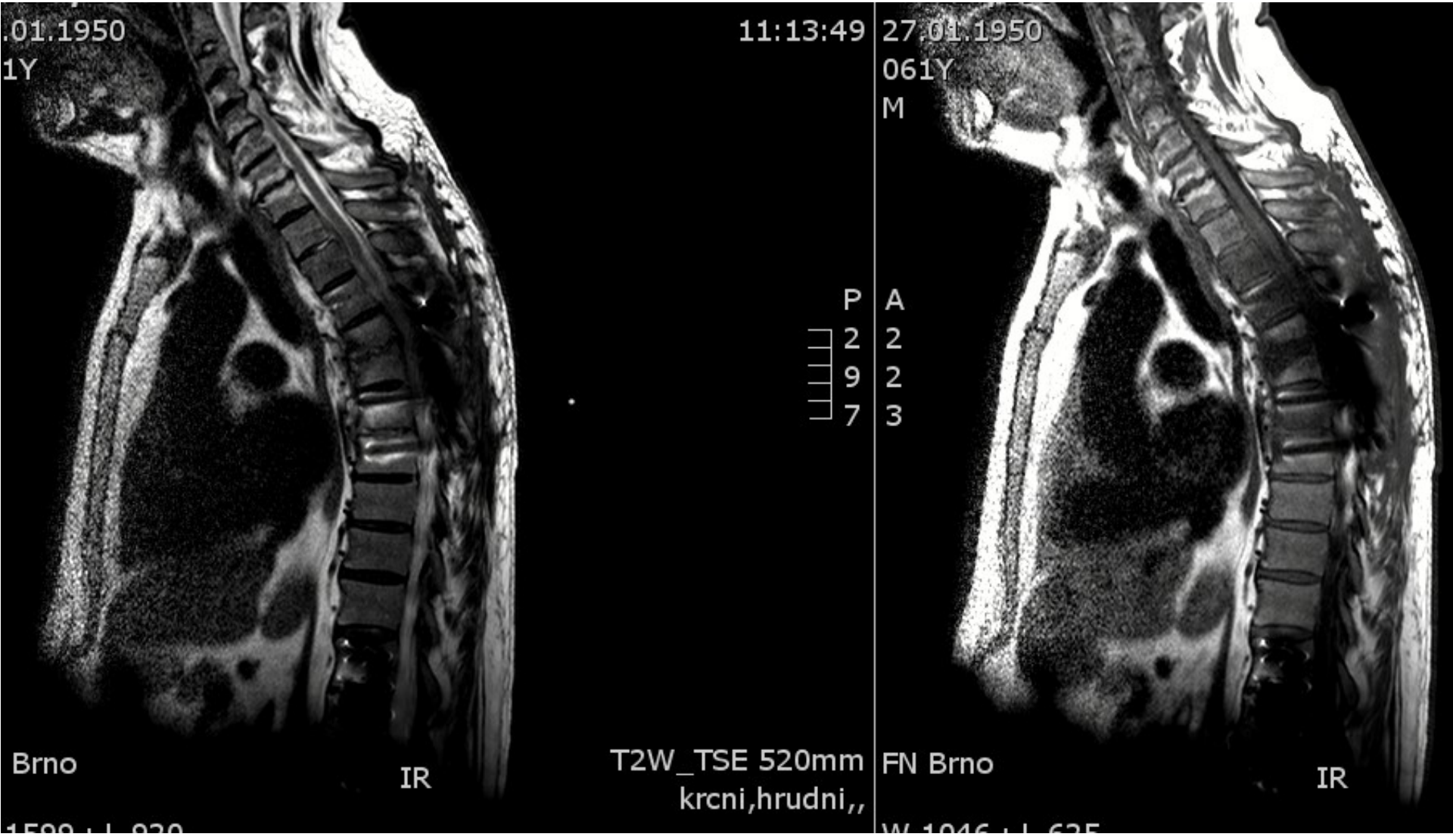

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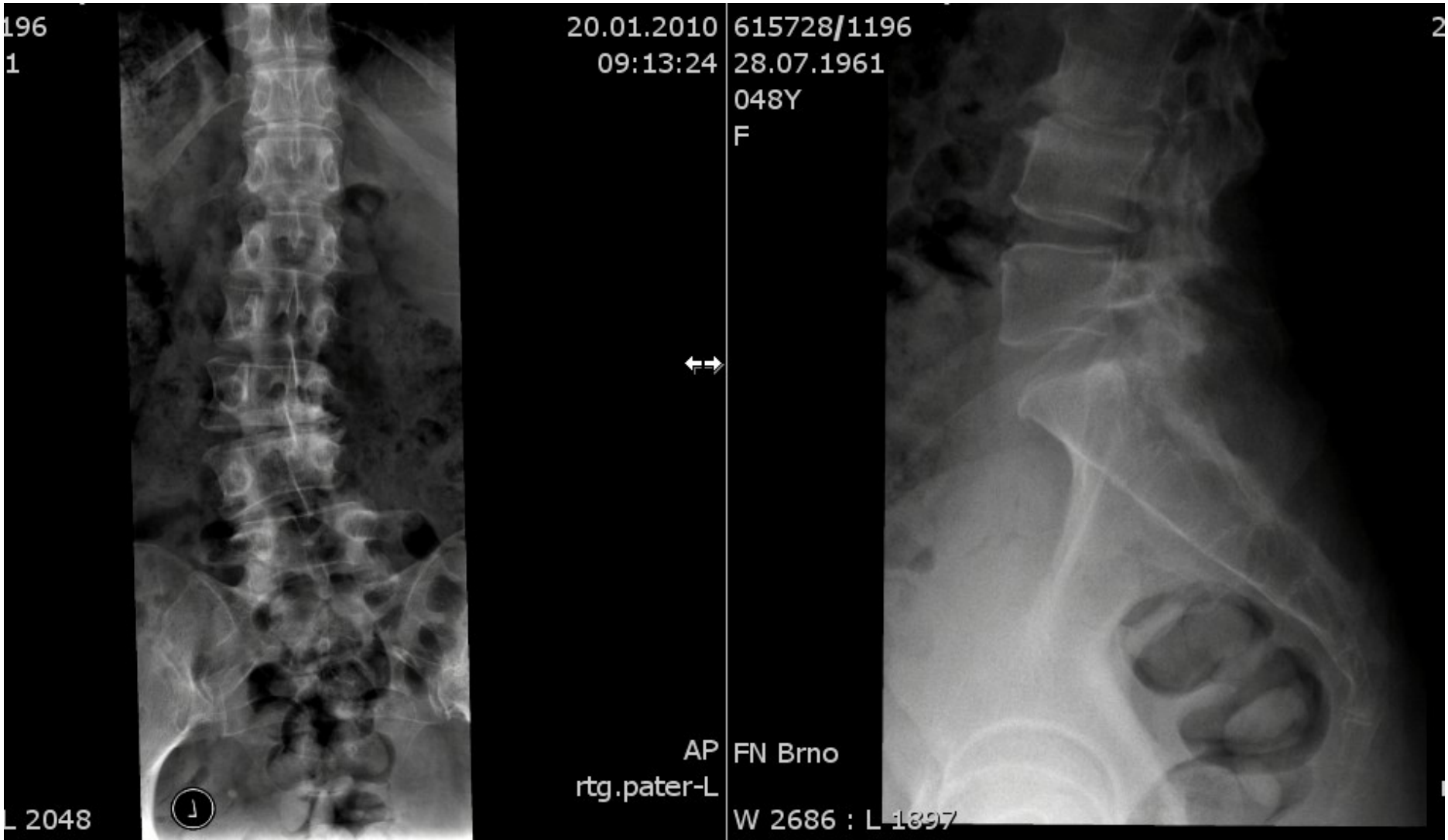
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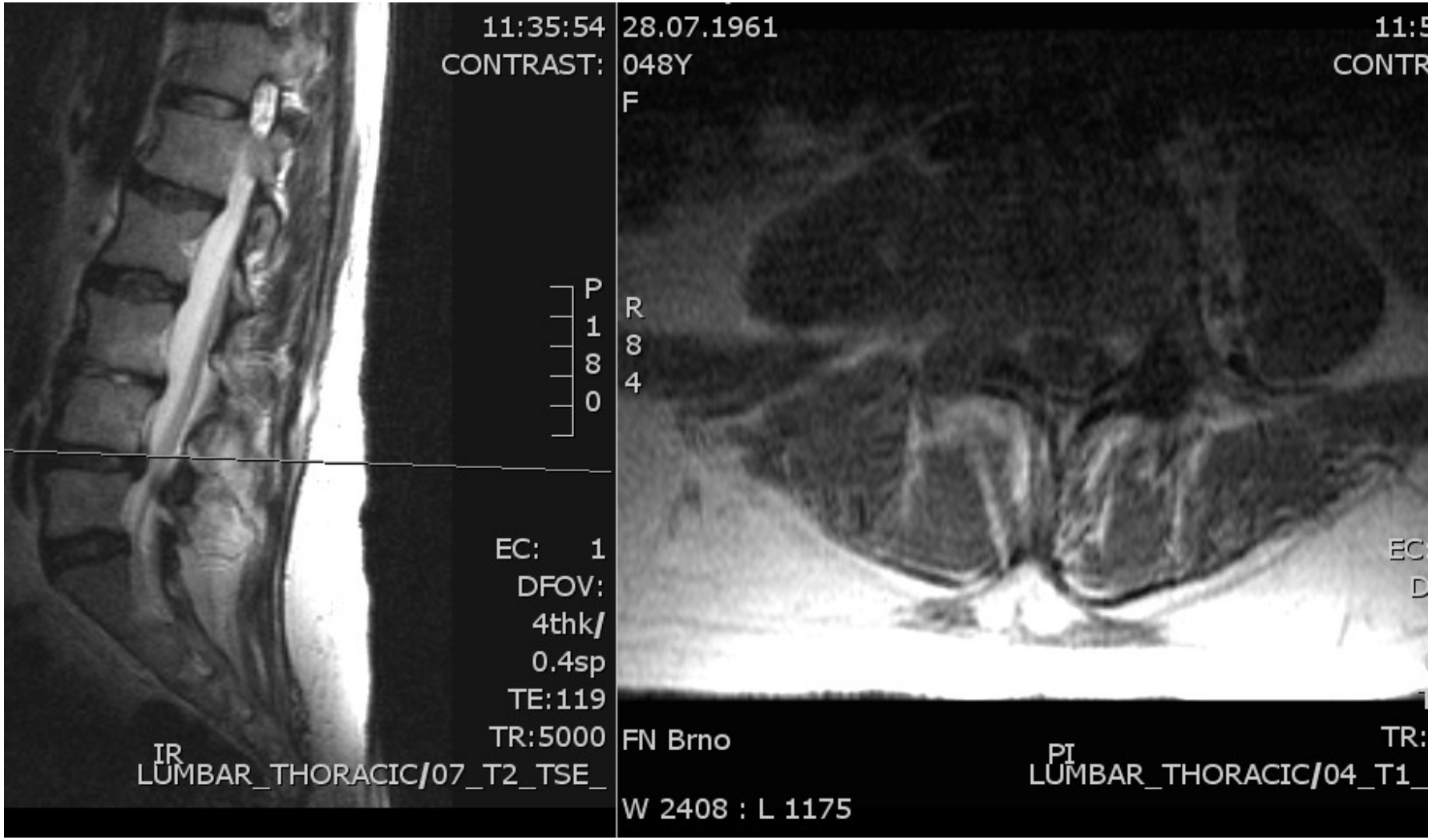
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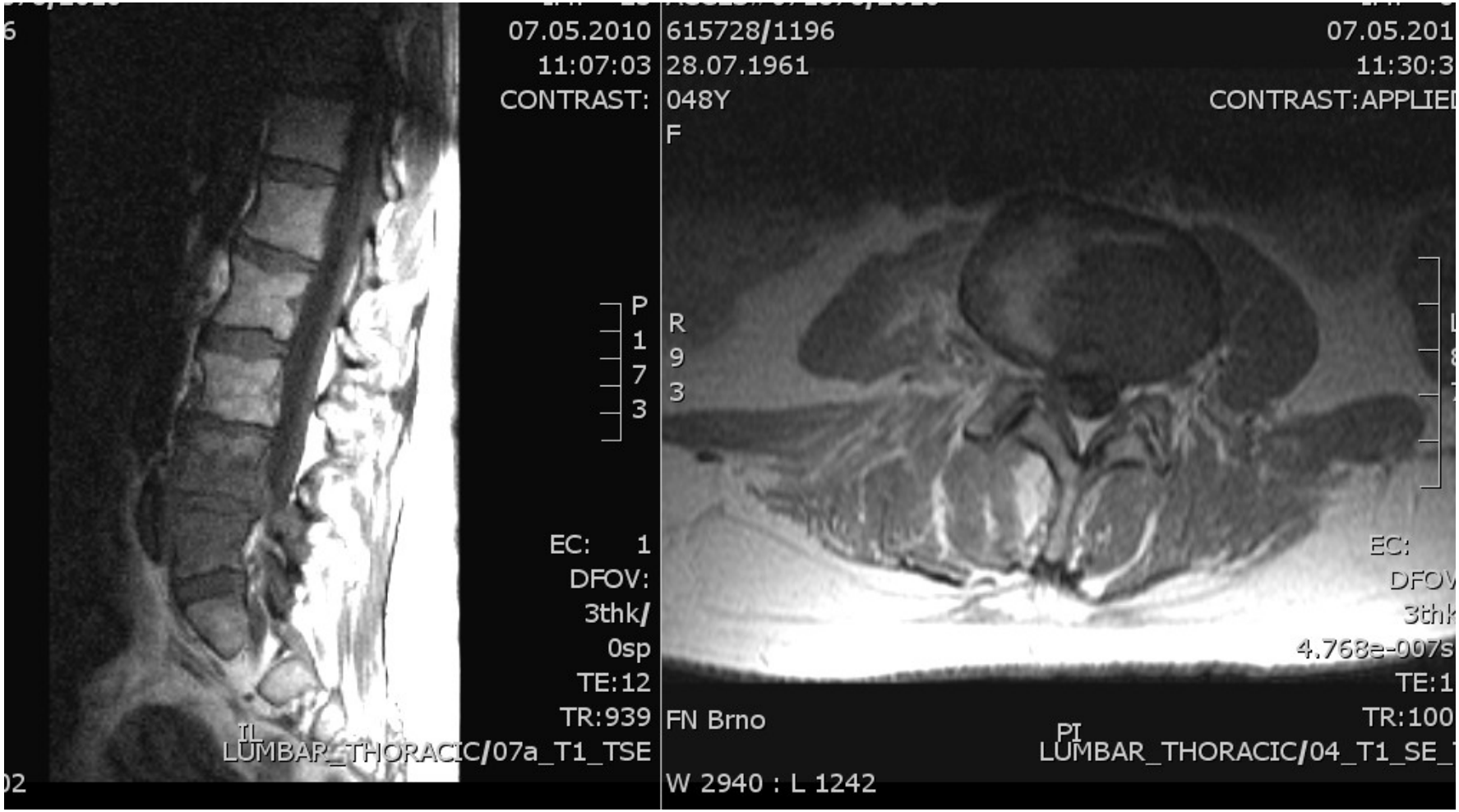
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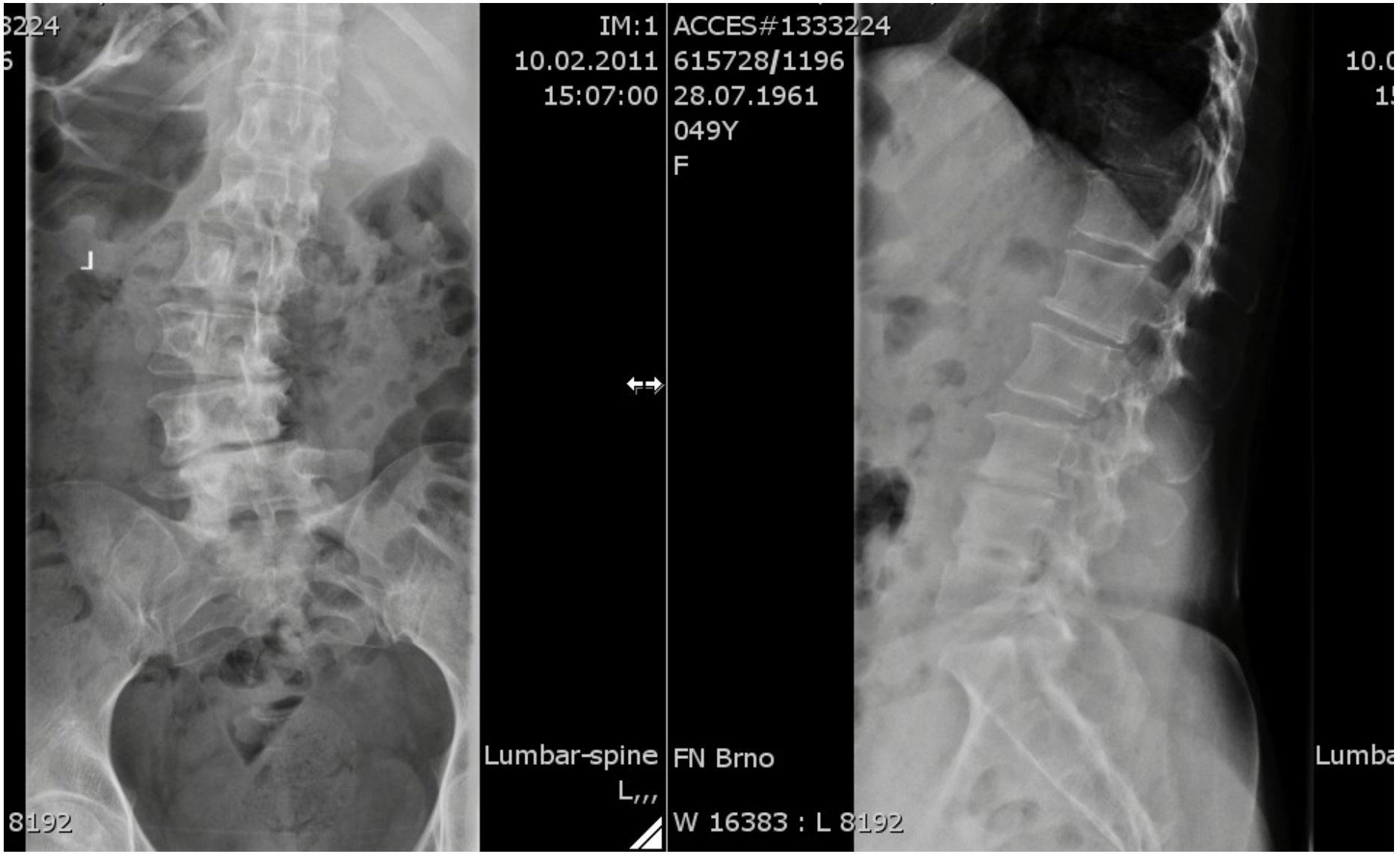
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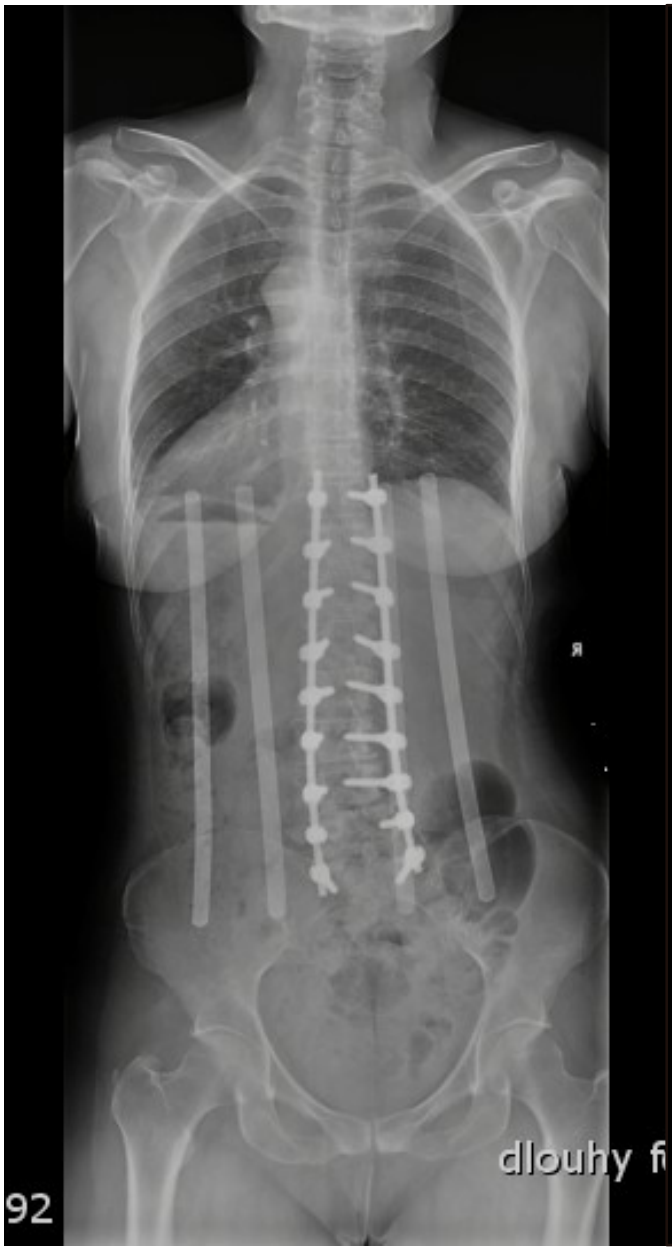
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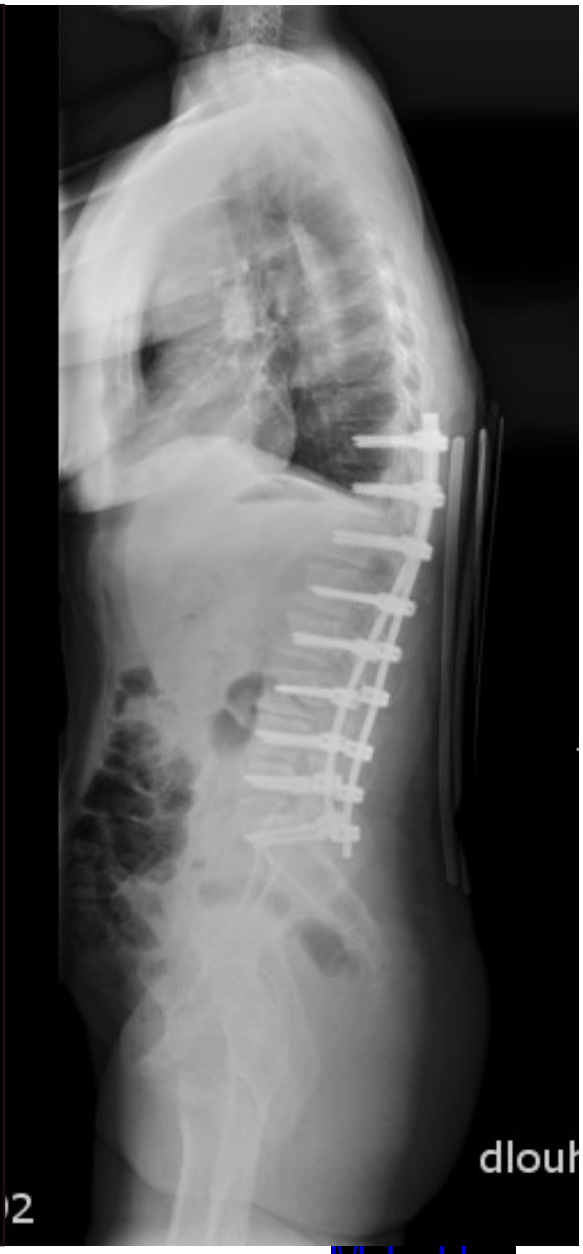
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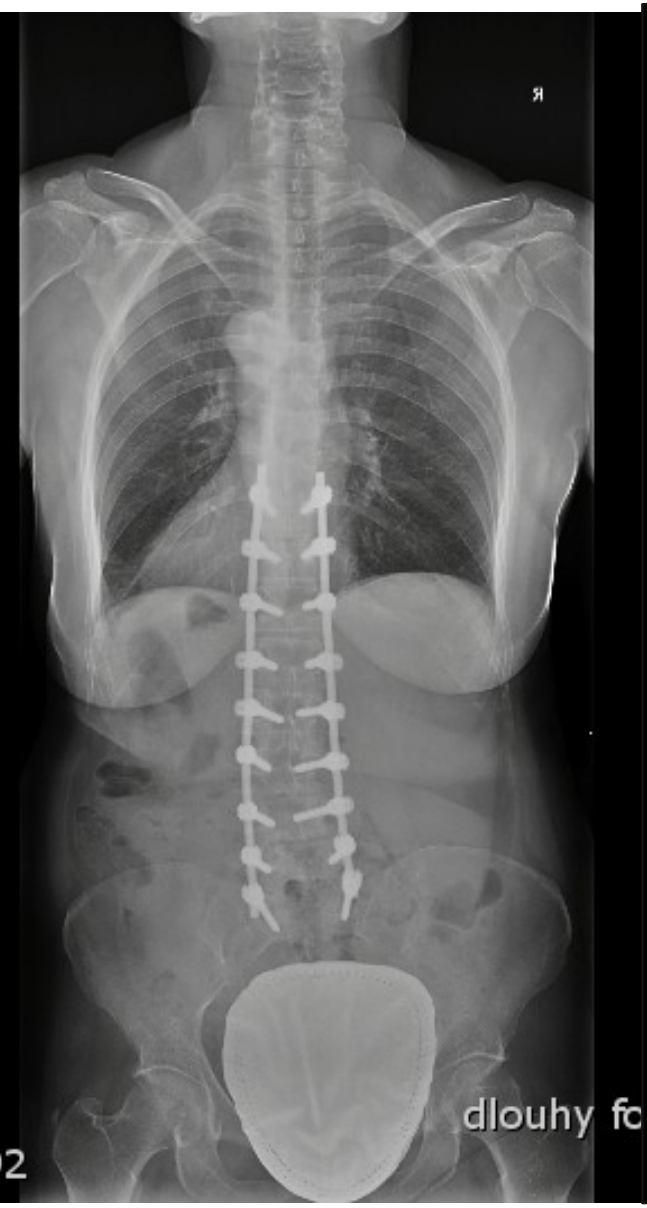

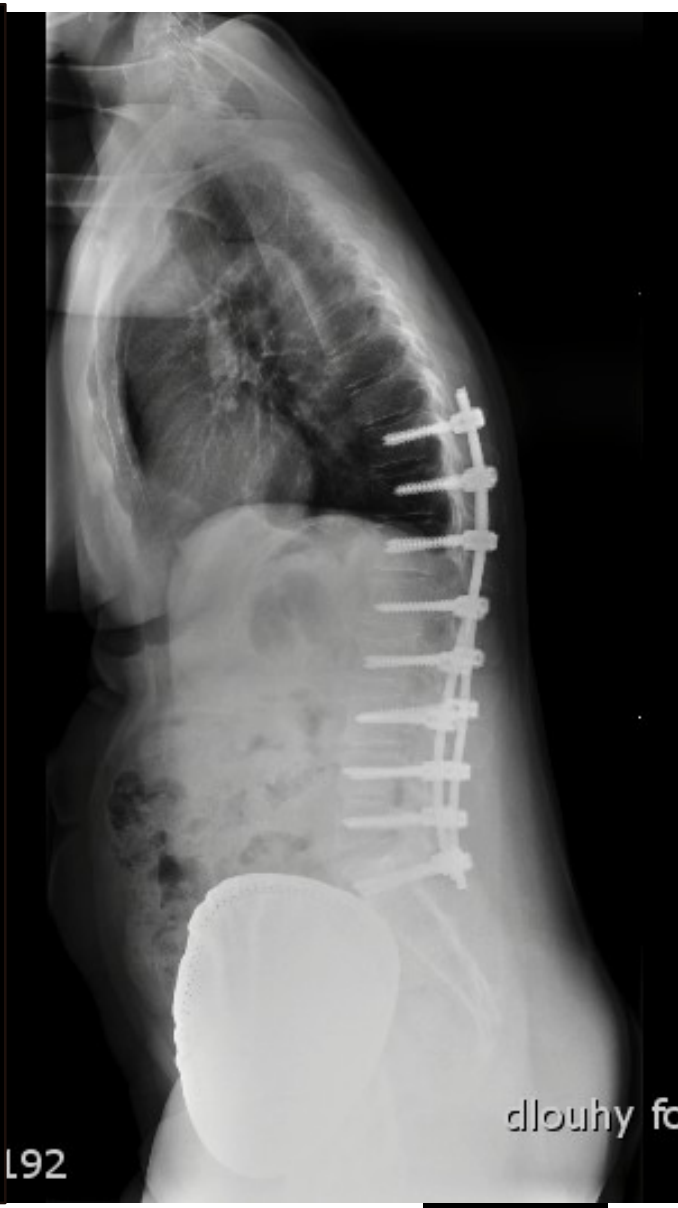

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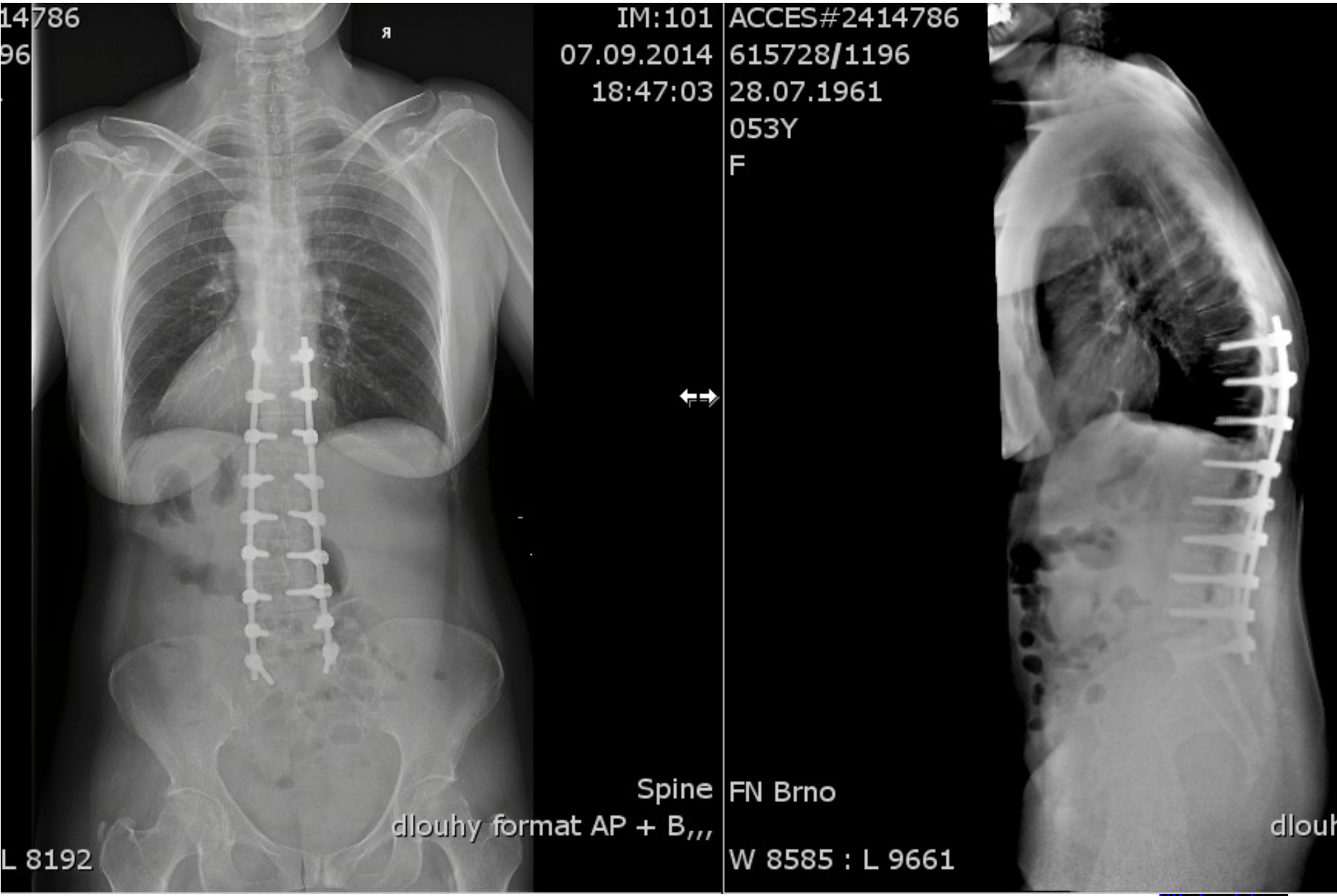
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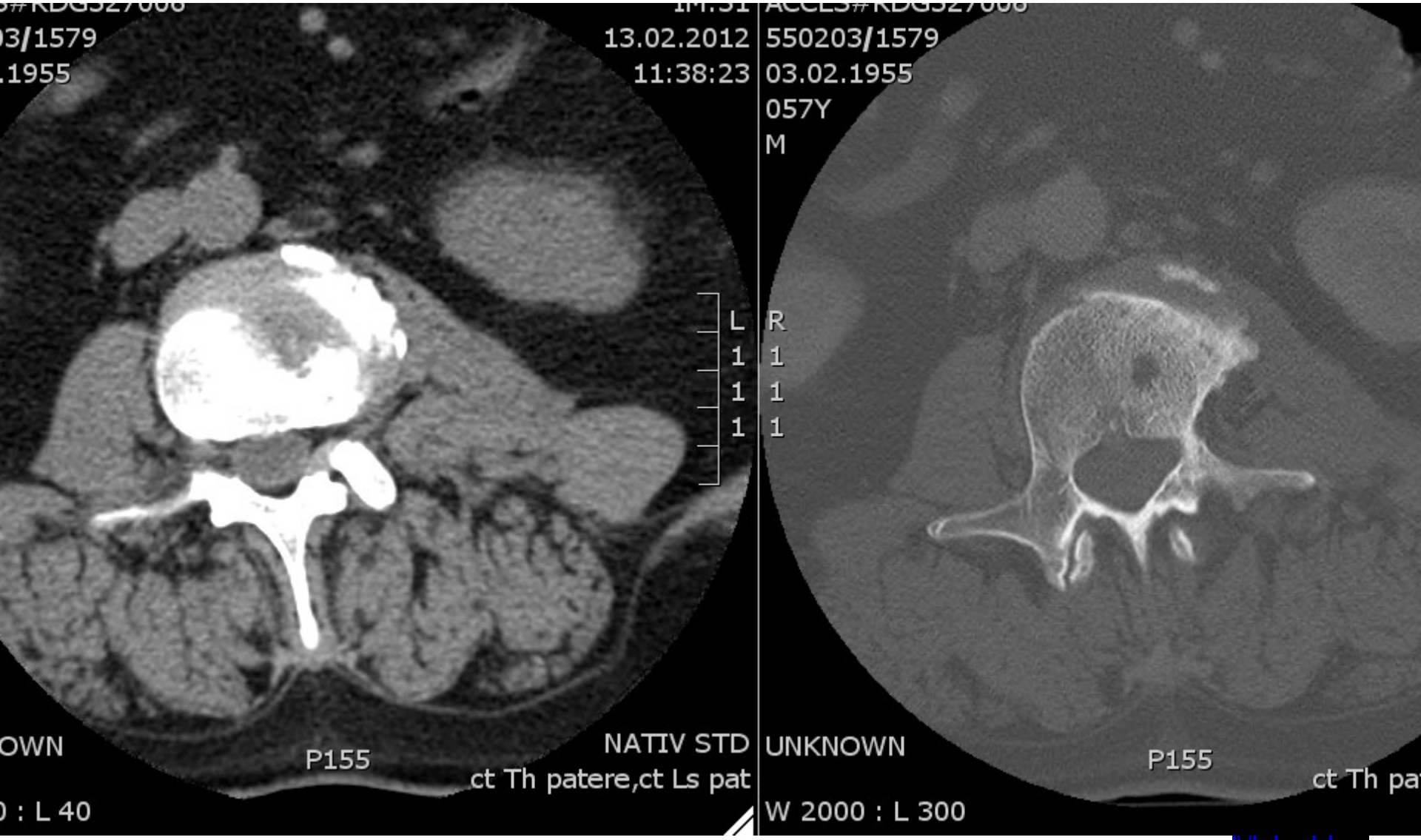
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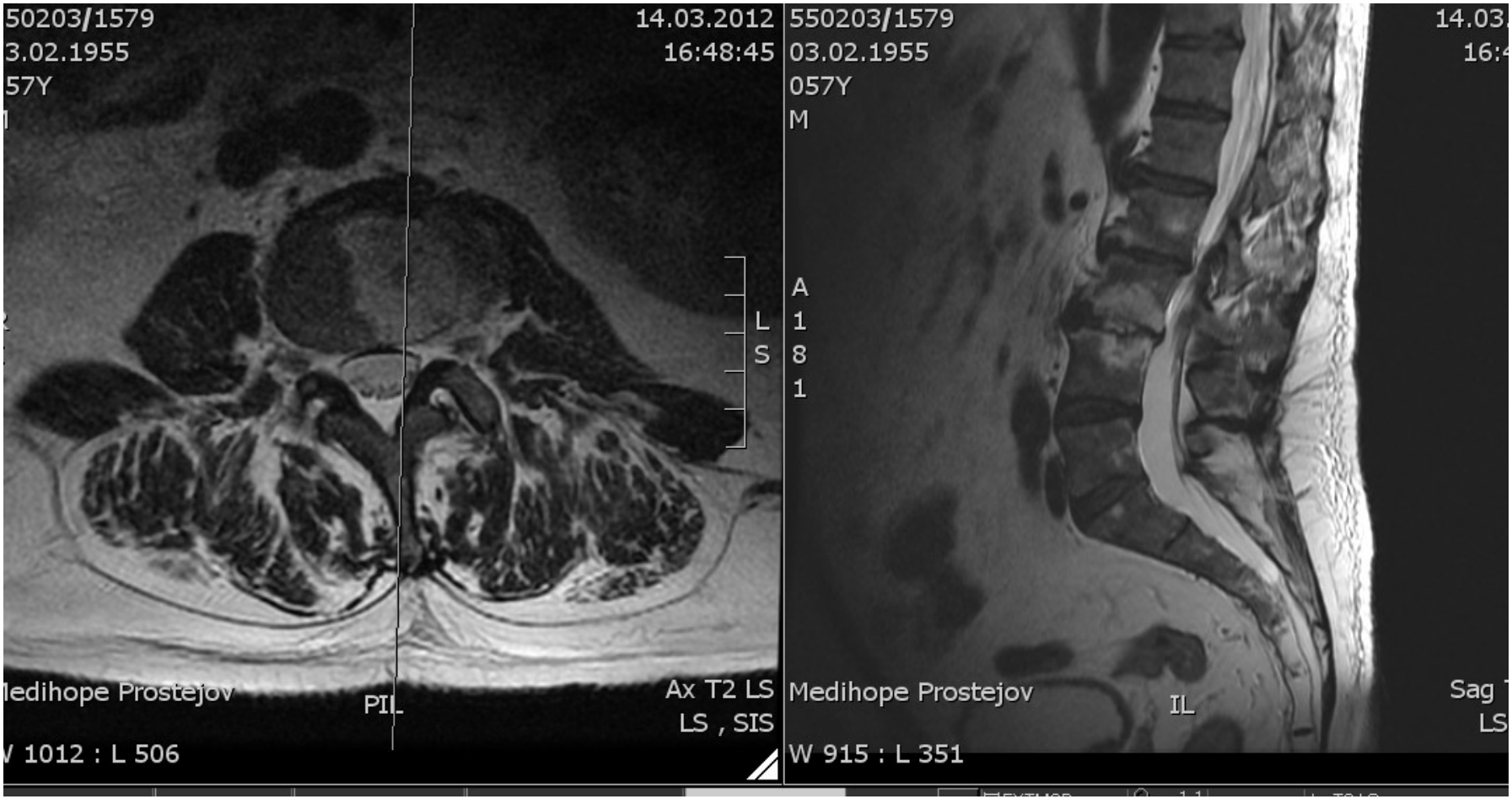
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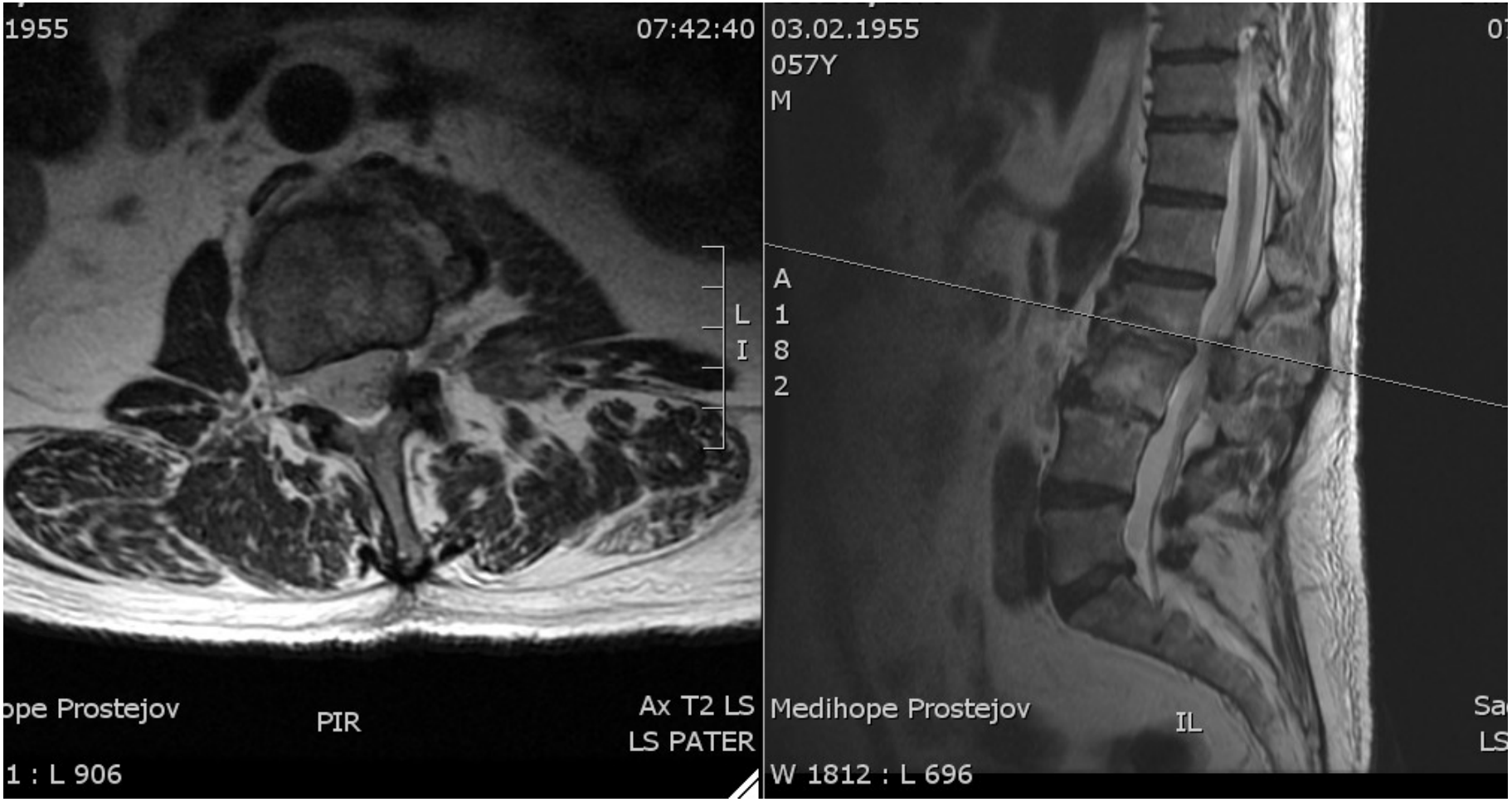
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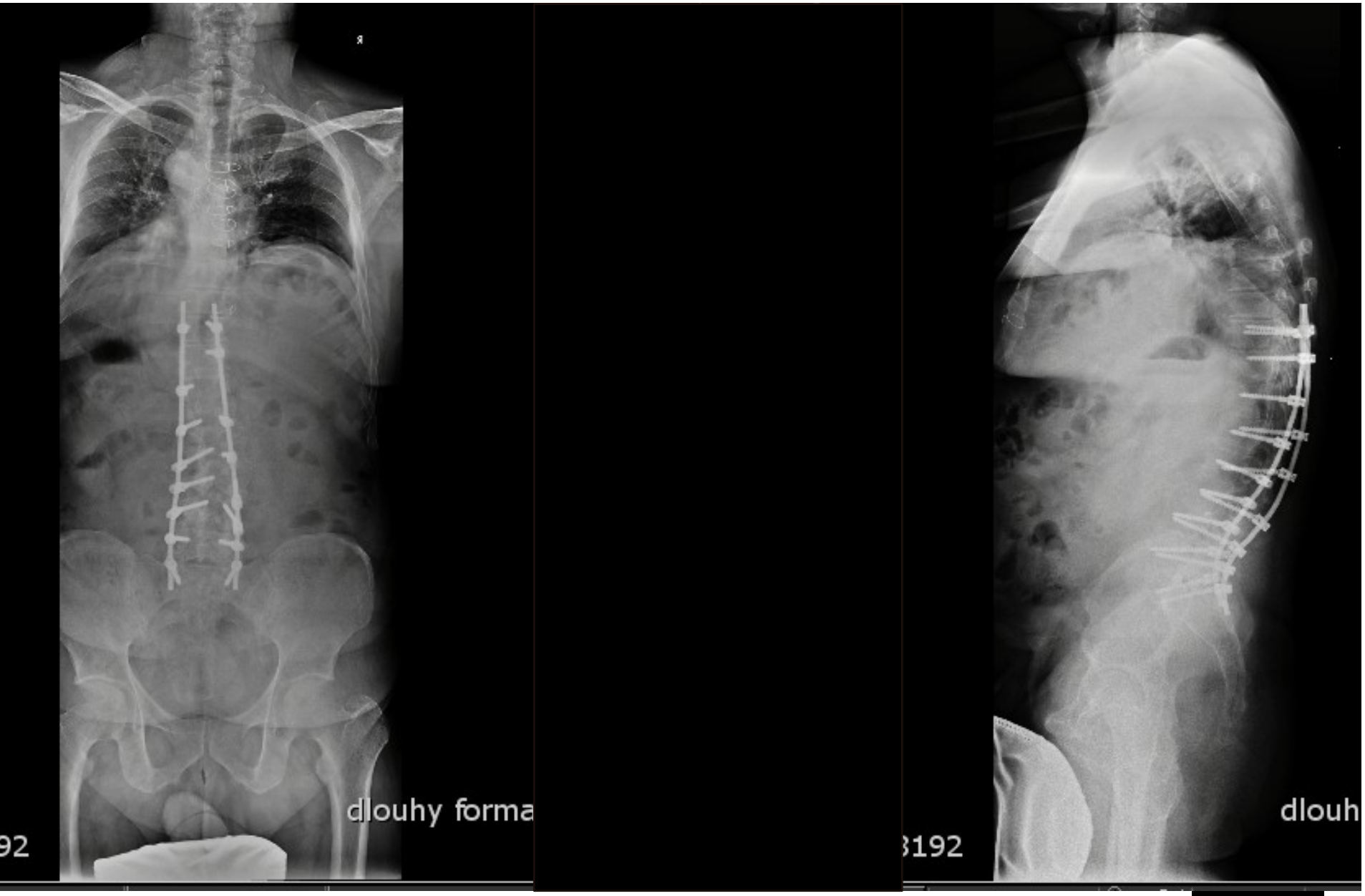
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Diagnostics – haemocultivation

- Haemocultivation sampling always **before ATB initiation** (risk of sterilisation of the cultures)
- Vessel selection: **aerobic** (*P. aeruginosa*, *Candida*), **anaerobic**: strict anaerobes, viridising streptococci
- **1 pair (concurrent collection) = 1 haemoculture (!)**
- 1 HMC is not enough, **ideally 2 to 3 sets**, sequential collection, increase of temperature / shivers
- In patients with CVC, at least one HMC from the catheter, other from periphery
- Vessel can be used also for CSF, centesis fluid, pus, exudate…

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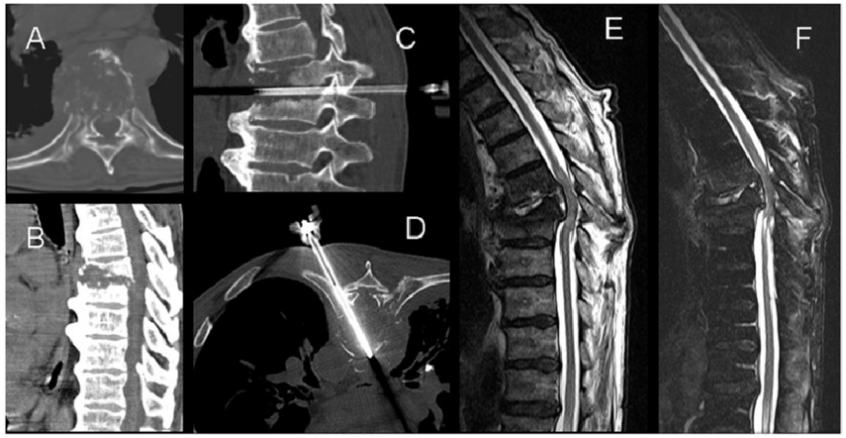
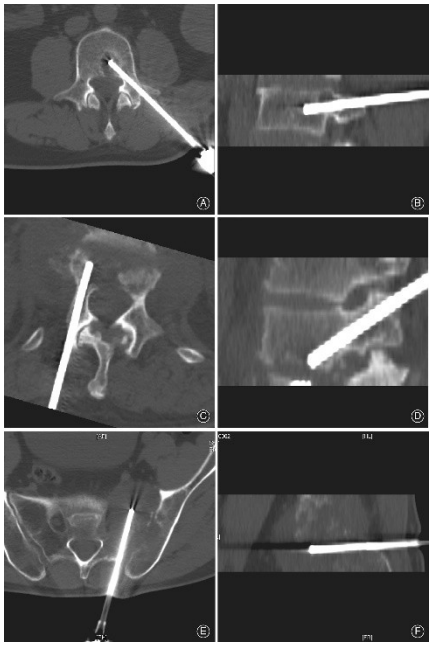
Diagnostics – biopsy

- Vertebral biopsy → targeted tissue collection from the lesion
  - For histology, cultivation, PCR diagnostics (bacteria, fungi)

- **Percutaneous CT-guided biopsy**
- **Open (surgical) biopsy**

- Indication:
  - Finding infectious agent when empirical ATB therapy fails
  - Ruling out neoplastic aetiology in differential diagnostics





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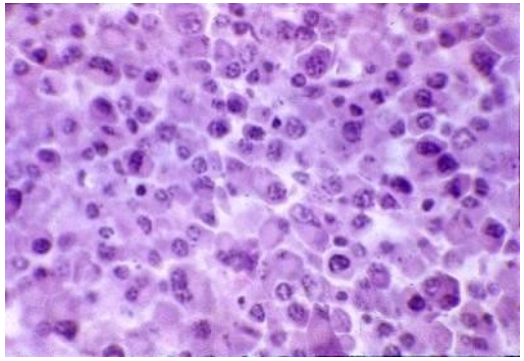
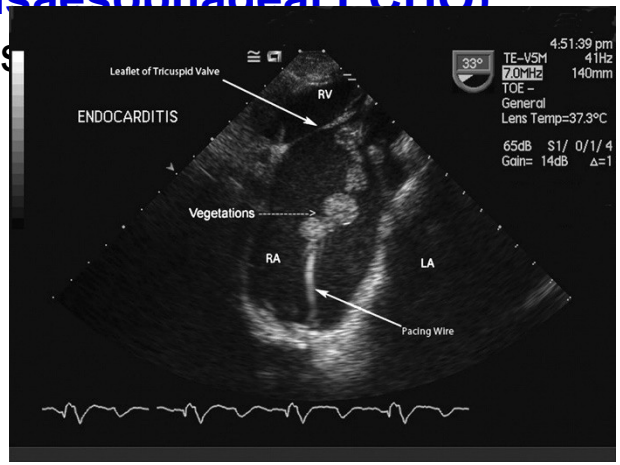
Differential diagnostics

- Erosive osteochondrosis
- Compressive vertebral fracture
- Neoplastic destruction
- Plasmocytoma
- Ankylosing spondylarthritis...



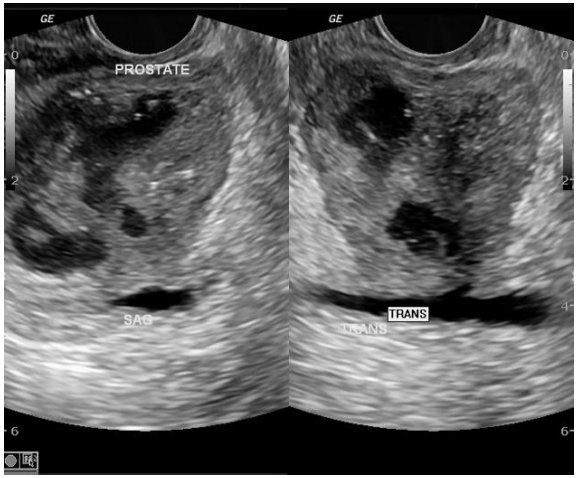
Vertebral plasmocytoma, Atlas of Pathology, University Hospital in Motol

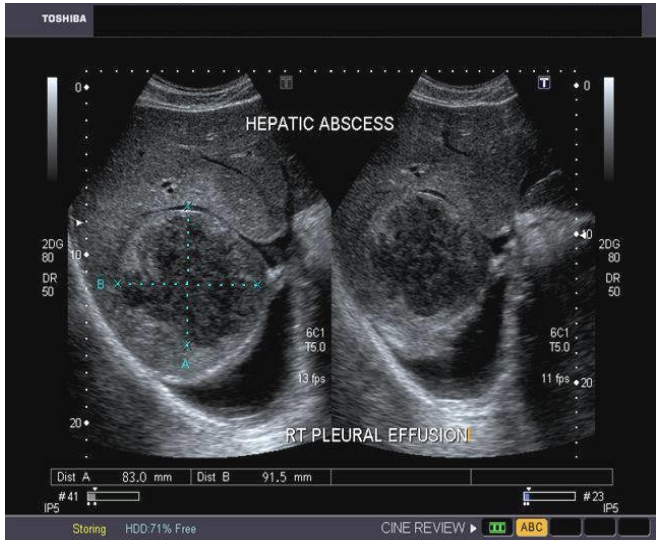
- Test to find the lesion = origin (always with ***S. aureus*** bacteraemia):
  - **Echocardiography (ideally transaesophageal ECHO)**
  - US of the abdomen and intestines
  - X-ray of the chest
  - **CT/MRI of the brain (abscess)**
  - Ocular fundus examination
  - US of soft tissues/CT

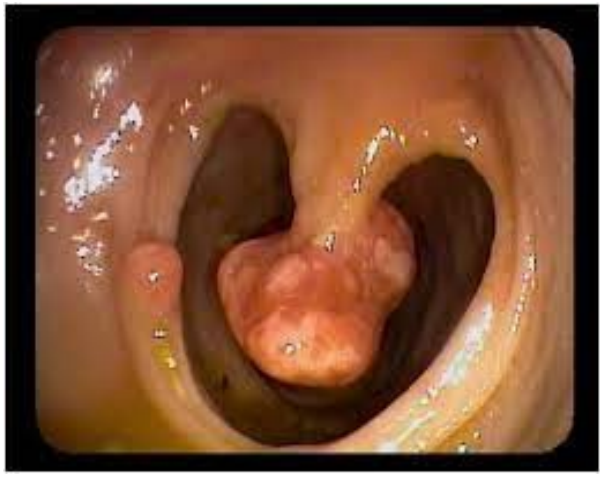


Differential diagnostics

- Proof of **G- aetiology** (enterobacteria) → search for origin in **GIT and UT**
  - US or CT of the abdomen
  - GFS, colonoscopy
  - CT IVU, cystoscopy, TRUS...







Treatment

- Always individual and multidisciplinary approach (!)

- We must consider:
  - **Neurological deficit**
  - The extent of involvement
  - Biomechanical instability of the spine
  - Conservative treatment failure
  - Always also comorbidities, **surgery risks**, patient's functional status

ECOG skóre	Biologický stav nemocného	Karnofsky index (%)
0	*schopen normální tělesné aktivity bez omezení*	90 – 100
1	*neschopen těžké fyzické námahy, ale může vykonávat lehčí práci*	70 – 80
2	*soběstačný, ale neschopen práce. tráví > 50 % denní doby mimo lůžko*	50 – 60
3	*omezeně soběstačný; upoután na lůžko > 50 % denní doby*	30 – 40
4	*odkázán na cizí péči; trvale upoután na lůžko*	20 – 30
5	*moribundní nemocný*	0 – 20

CONSERVATIVE
x
SURGICAL

ATB therapy

Bactericidal ATB of the blood component, initially empirical, then targeted to the cultivated agent and **its ATB susceptibility** (MRSA, ESBL, MBL strains...)

Always **long-term**, parenteral for the first 2–4 weeks, oral after stabilisation

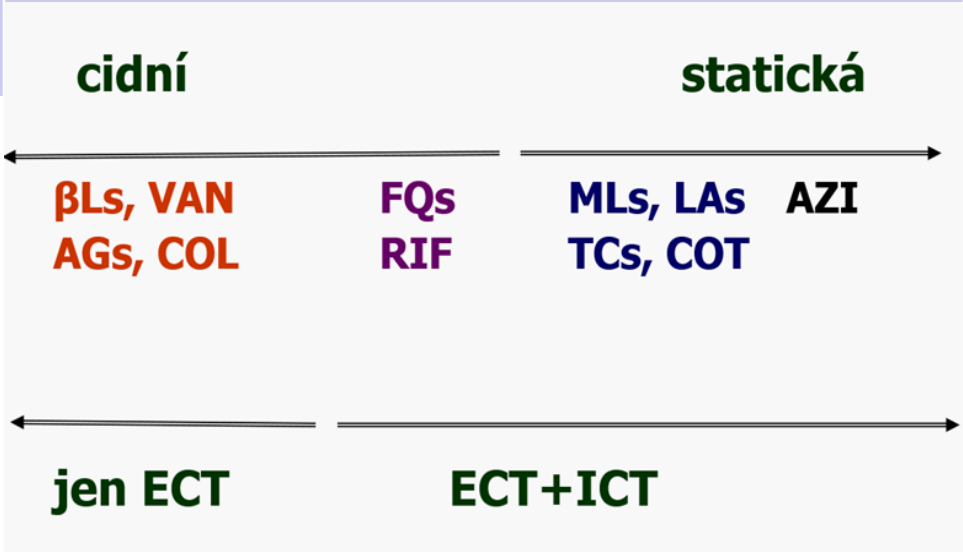
12 weeks is the gold standard, recent tendency to shorten ATB period

On-going clinical check, inflammatory parameters, imaging examinations (MRI after a time, gradual regression)

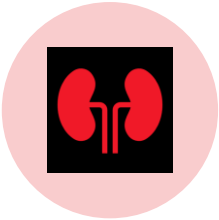
Consider **ATB toxicity risks**, induction of Clostridium colitis, allergies...

ATB therapy

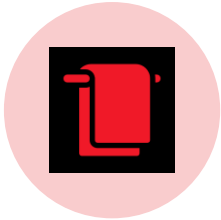
Targeted according to haemocultivations	Empirical ATB therapy
Staphylococci: 1. Oxacillin IV 16–20 g/day 2. Vancomycin IV (MRSA) 30 mg/kg/day 3. Linezolide IV	**Initial parenteral:** Oxacillin (vancomycin) + gentamicin, rifampicin Carbapenems (meropenem) Vancomycin + 3rd or 4th generation cephalosporin (or fluoroquinolone)
Enterobacteria, G- bacilli 1. 3rd or 4th generation cephalosporins 2. Combination with aminoglycosides 3. Monotherapy with carbapenems	**Following oral:** Cotrimoxazole + rifampicin (affects biofilm) Doxycycline Clindamycin, cefuroxime axetil, linezolide...
Streptococci: G-PNC, cephalosporins...	



Conservative treatment



Initial therapy usually **during hospitalisation**, then outpatient follow-up (INF + ORT)



Sufficient **analgetisation**

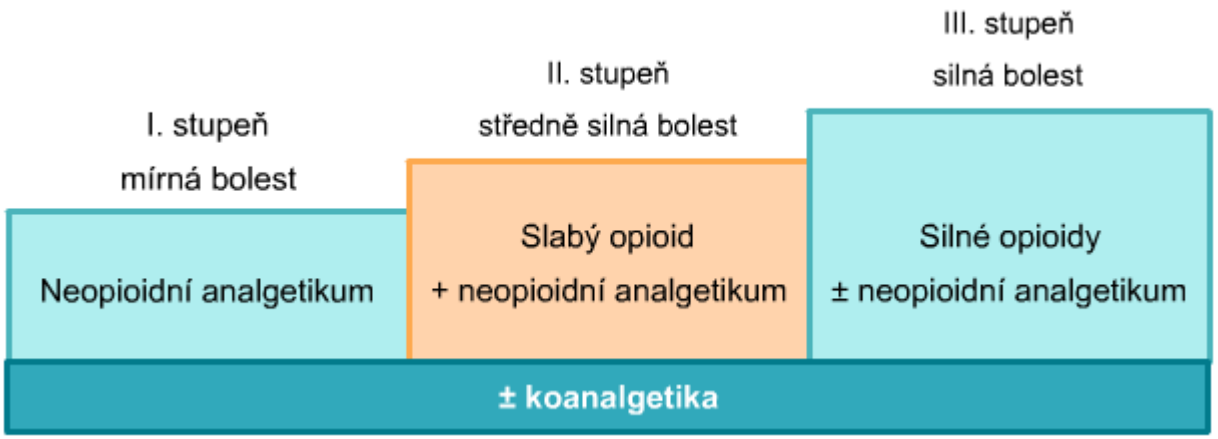
- Paracetamol + tramadol
- Opiate patches
- Co-analgesics
- Via outpatient pain treatment

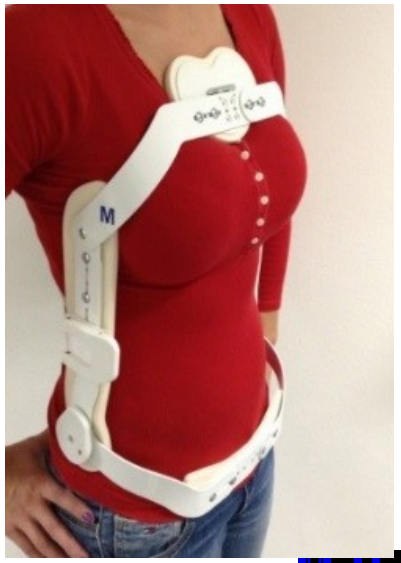
Comprehensive care for internal environment, **TED prophylaxis**, adequate nutrition, probiotics...

Initially typically resting regimen, gradually RHB, **spinal immobilisation** (Jewett brace, lumbar brace, cervical collar...)

Conservative treatment

- ATB therapy
- Analgesia
- Braces
- Targeted RHB





Surgical treatment

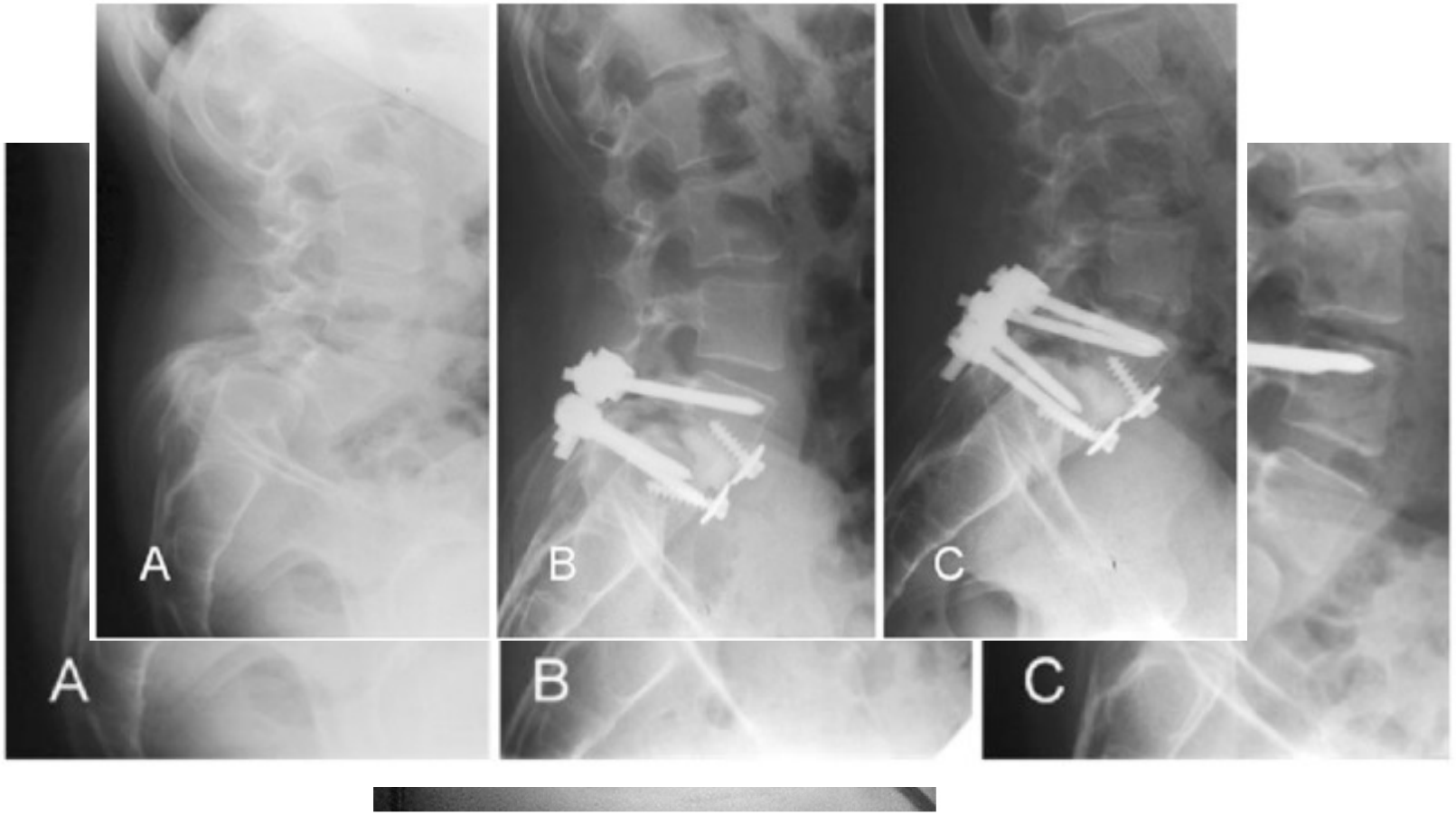
Traditional open procedures:

- Posterior/anterior/lateral stabilisation and decompression
- Auto/allografts
- Instrumentation

MISS:

- Percutaneous drainage of the abscess, transpedicular biopsy and drainage
- Percutaneous transpedicular stabilisation w/out debridement, decompression
- Frontal minimally invasive approach and debridement, spondylodesis w/out instrumentation (mini-open or endoscopic)
- Combination of procedures

Magerl fixator



Case study 1

Medical history:

- Male, 74 years, retired, history of internal jugular vein thrombosis with CVC
- status post left-sided hemicolectomy + cholecystectomy due to colorectal adenocarcinoma in 1998; also status post stercoral peritonitis with bowel perforation and septic shock development, jejunostomy performed in 2016
- Short bowel syndrome, **long-term supplemental PE nutrition via PICC**
- LMWH chronic prophylaxis

Present complaint:

- 3/2019 hospitalised at Internal Medicine Dept., catheter sepsis, oxacilline-resistant *S. epidermidis* aetiology, ATB combination **ceftriaxon + clindamycin**, PICC kept, discharged home

- 6/2019 new hospitalisation at the Neurology Dept. for **lumbar spine pain** (chronic, recently worsening), propagating into his left side and abdomen, at home sometimes chills, subfebrile temperatures, resolving with paracetamol

Case study 1

Laboratory on admission:
WBC 7.7 x 10^9/L, **PLT 147 x 10^9/L**, **Hb 91 g/L**, **CRP 72 mg/L**, PCT 0.1 ng/L

Haemocultivation: G+ cocci, oxacillin-resistant ***S. epidermidis***

Suspected lesion is the **PICC (in place for 2 years)**, empirical ATB **vancomycin IV**

ECHO without a proof of IE, abdominal US without a pathological finding, heart + lungs X-ray without infiltration

MRI of Th-L spine **– image of Th10 and 11 spondylodiscitis with epidural perivertebral infiltration on the left, no proof of abscess**

ATB therapy escalated to **vancomycin + clindamycin IV**

PICC kept in situ (!)

Case study 1

Vancomycin discontinued after 14 days, oral clindamycin maintained

Fevers recur 6 days after vancomycin discontinuation, lab. CRP 50

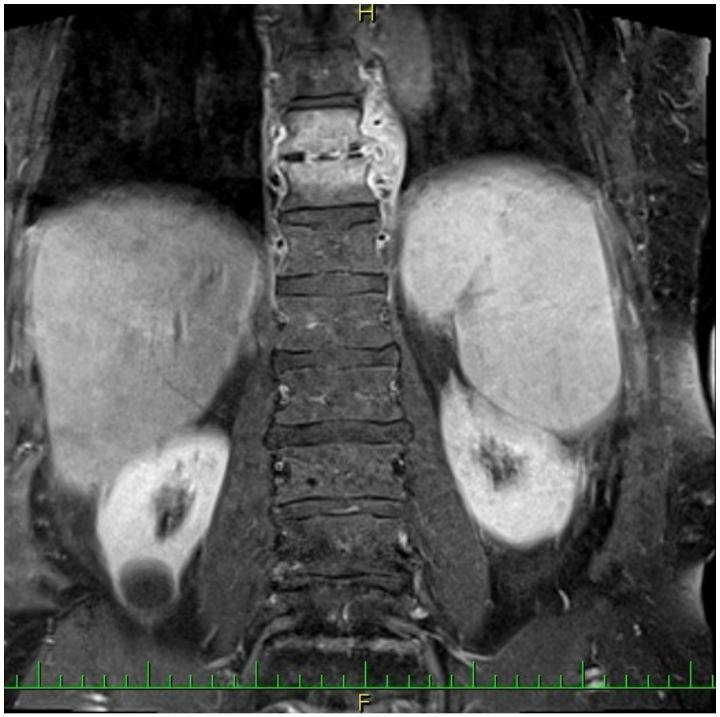
ATB therapy changed to **clindamycin + levofloxacin**

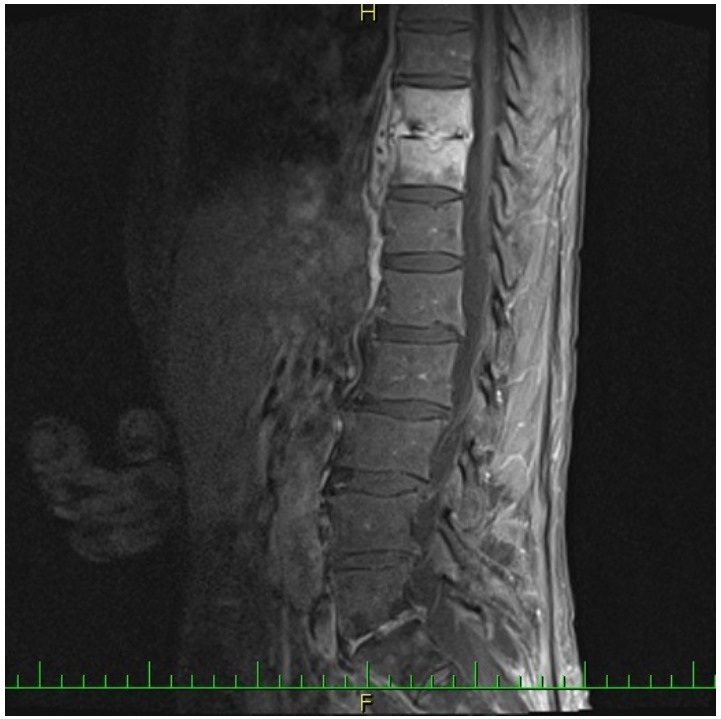
Search for lesions resumed: X-ray of the heart + lungs, paranasal sinuses, MRI of the brain and C spine, ORL and stomatological examination – no infectious lesion.

Follow-up MRI of the spine after 1 month:

Progression of Th10/11 spondylodiscitis, vertebral bodies completely involved, progression of perivertebral infiltration on the right with a small abscess ca 4 mm

Case study 1



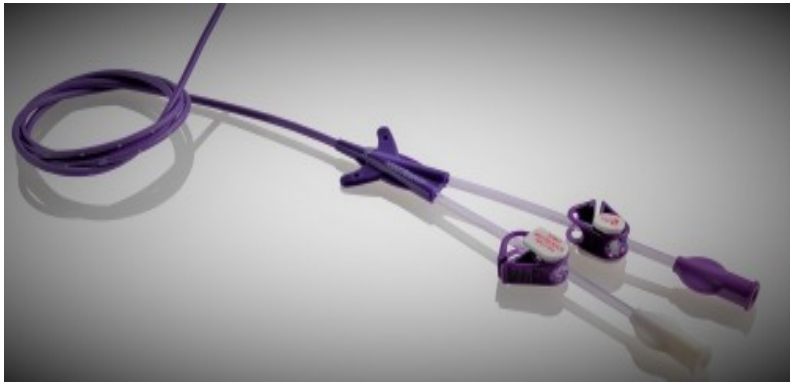


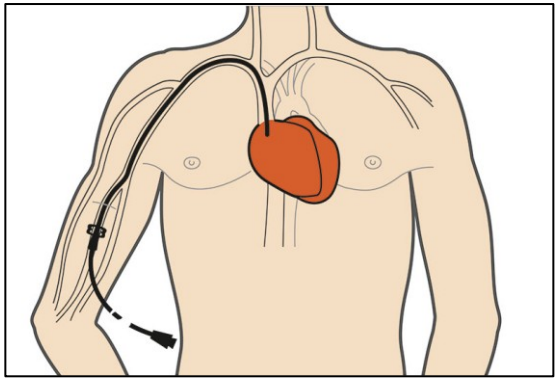
Progression of Th10/11 spondylodiscitis, vertebral bodies completely involved, progression of perivertebral infiltration on the right

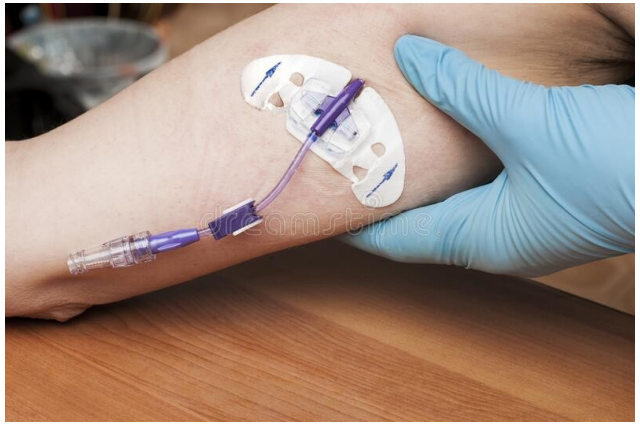
Case study 1

8/2019 transfer from regional Neurology to the Clinic of Infectious Diseases

- PICC extraction (after > 5 weeks of ATB treatment, a replacement introduced through the left cephalic vein)
- Continuing **clindamycin + levofloxacin** ATB therapy







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Case study 1

Five days after PICC replacement, the patient is **febrile again, elevated CRP**, low procalcitonin

On day 6 **swelling of the upper left limb** – according to US, a complete **thrombosis** of v. cephalica, spreading to v. axillaris, thrombosis of v. subclavia, including vasculature in the subclavicular region.

The thrombotised PICC extracted, a tunneled Hickman catheter introduced via the left internal jugular vein at the angiography suite, ATB escalated to **meropenem + fluconazol**e, LMWH

Follow-up MRI of the spine after 9 weeks of ATB treatment – **status post spondylodiscitis Th 10/11, no epidural abscess, inflammatory changes regression**

ATB therapy 1 more month **oral levofloxacin**, **total of 10 weeks hospitalisation**

Patient is further afebrile, without a neurological deficit, CRP below 5

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Case study 1 – summary

Complications in 11/2019 – primary attack of enterocolitis caused by *C. difficile*

ATB history:
Ceftriaxon, clindamycin, vancomycin, levofloxacin, meropenem, fluconazole

Early extraction of a foreign body as the source of bacteraemia

Rationalisation of ATB therapy, a candidate for an OPAT regimen therapy (dalbavancin – ideal choice for oxacillin-resistant staphylococci)

OPAT (*Outpatient Parenteral Antimicrobial Therapy*)

Continuing ATB therapy is usually necessary after discharge from hospitalisation

a) A suitable oral drug exists → **always prefer oral ATB**
b) No oral drug (agent + susceptibility, allergy...) → continue hospitalisation

...or OPAT!

ATB regimens suitable for outpatient parenteral therapy **of skeletal infections**:

- Amikacin, gentamicin **1x daily IV** (multiresist. *Pseudomonas aeruginosa*)
- Ertepenem **1x daily IV** (ESBL strains of enterobacteria)
- Teicoplanin **3x weekly IV** (G+ cocci)

- **Dalbavancin** 1x weekly IV (MRSA, coagulase-negative staphylococci)
  → Lipoglycolpeptide ATB, biological half-life ca 180 hours
  → Lipophilic chain – good tissue penetration
  → Inhibits growth and multiplication of G+ bacteria 10x stronger than vancomycin

OPAT

KDO JE TO?

Opat

OPAT advantages:

- Shortened hospitalisation
- **Reduced risk of nosocomial infections** and other complications
- Earlier restoration of mobility, **return to regular activities**, earlier RHB

OPAT disadvantages:

- **Who, where and how will apply it?**
- The economical paradox – shortened hospitalisation according to DRG is often a disadvantage
- ATB suitable for OPAT (dalbavancin) **is expensive**, approval by physician reviewer
- Supervision concerning development of complications, recurrent disease...
- **Secured venous access (peripheral x central x PICC x midline catheter)**

Discussion

- Diagnostic **delay** (the interval from onset of complaint to determination of the correct diagnosis) is **10 weeks on average** (2 to 6 months)!

- **Mortality and the presence of permanent neurological consequences both correlate with the delay in establishing the correct diagnosis**

The 50% rule

- ✓ **50%** of patients are over 50 years old
- ✓ Fever is present in **50%** of cases
- ✓ Physiological peripheral blood leukocyte count is present in **50%** of cases
- ✓ *Staphylococcus aureus* is the aetiological agent in over **50%** of cases
- ✓ Lumbar spine is involved in **50%** of cases
- ✓ The primary lesion is not found in **50%** of cases
- ✓ The symptoms last over 3 months in **50%** of patients

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