University Hospital
Heidelberg

US, CT and MRI in CE

Thomas Junghanss, Marija Stojkovic

Clinical Tropical Medicine Unit

Waldemar Hosch, Tim Weber

Department Radiology

WAE

Lima 2019

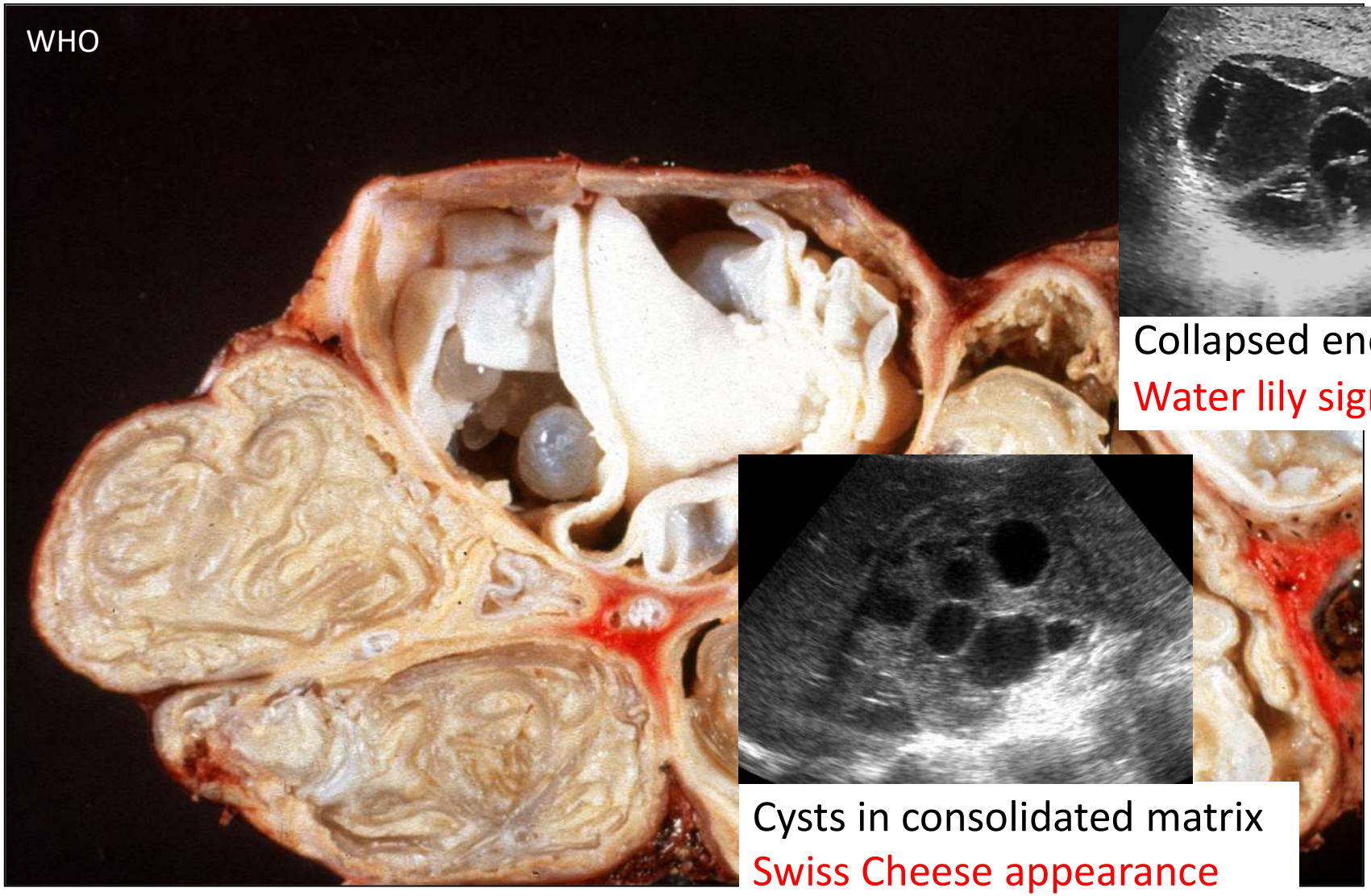
Translating cyst architecture into imaging


WHO
WHO

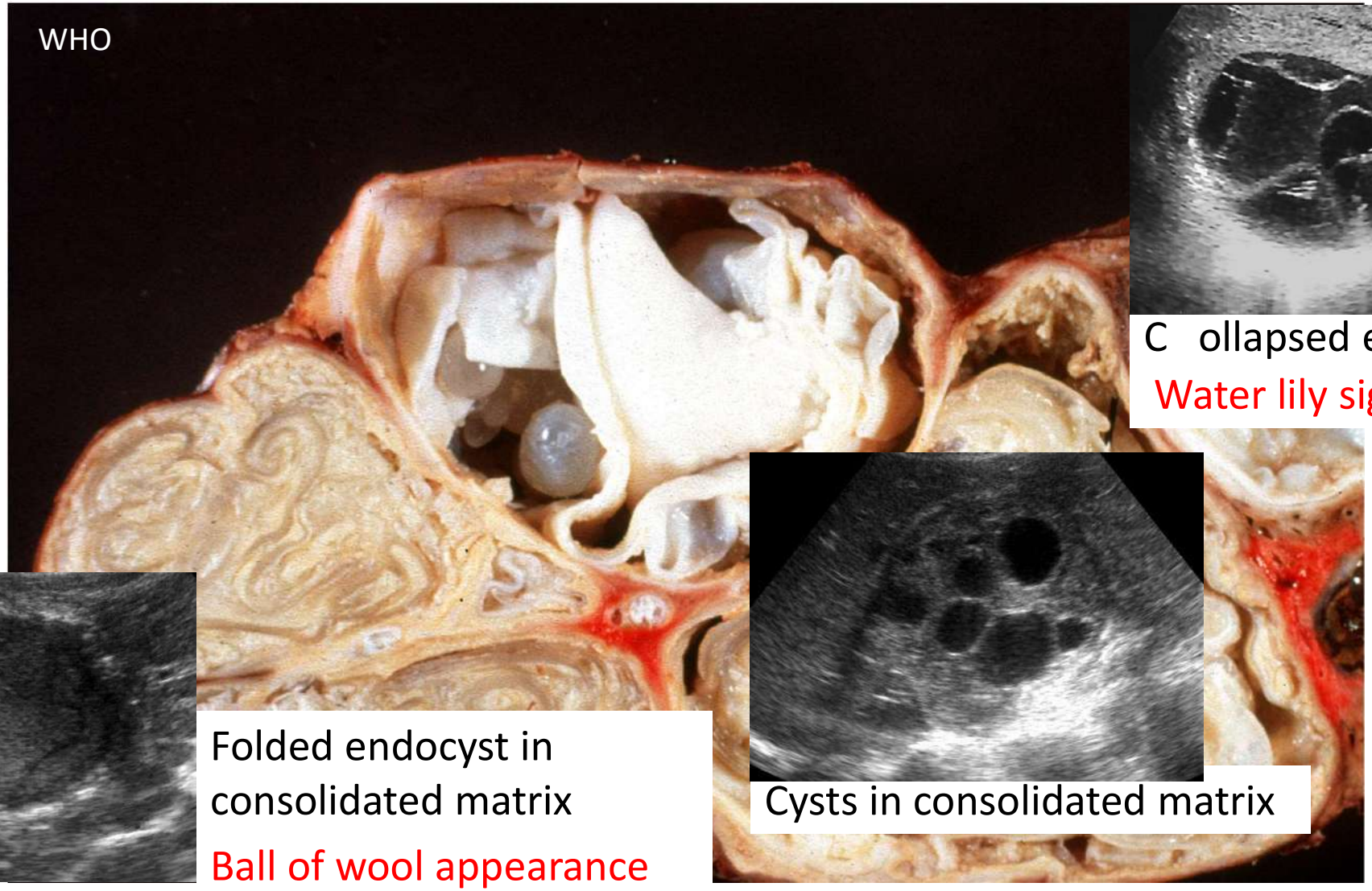
Collapsed endocyst

Water lily sign

Image: Heidelberg University Hospital



Images: Heidelberg University Hospital



C ollapsed endocyst

Water lily sign

Folded endocyst in consolidated matrix

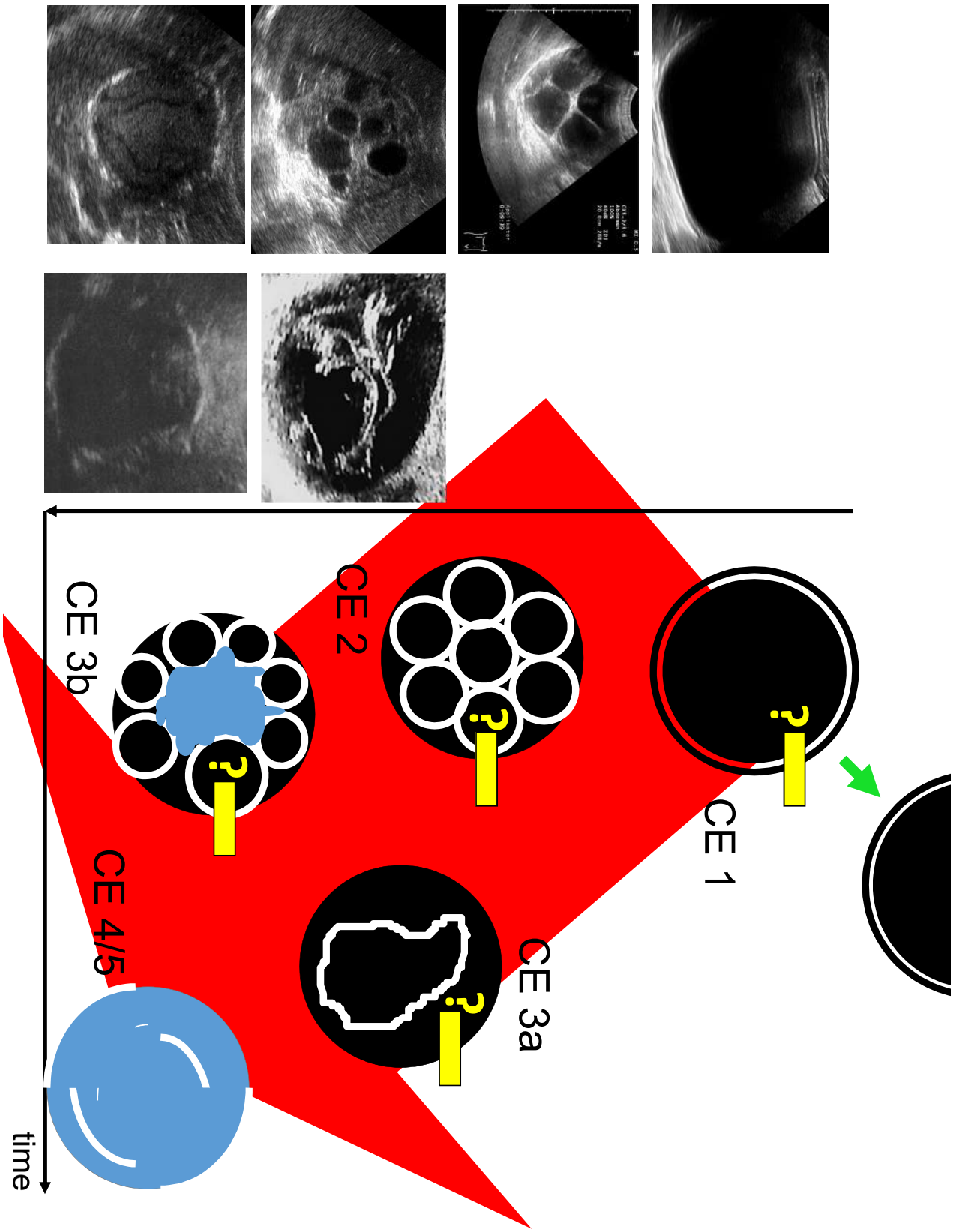
Ball of wool appearance and canalicular structure

Cysts in consolidated matrix

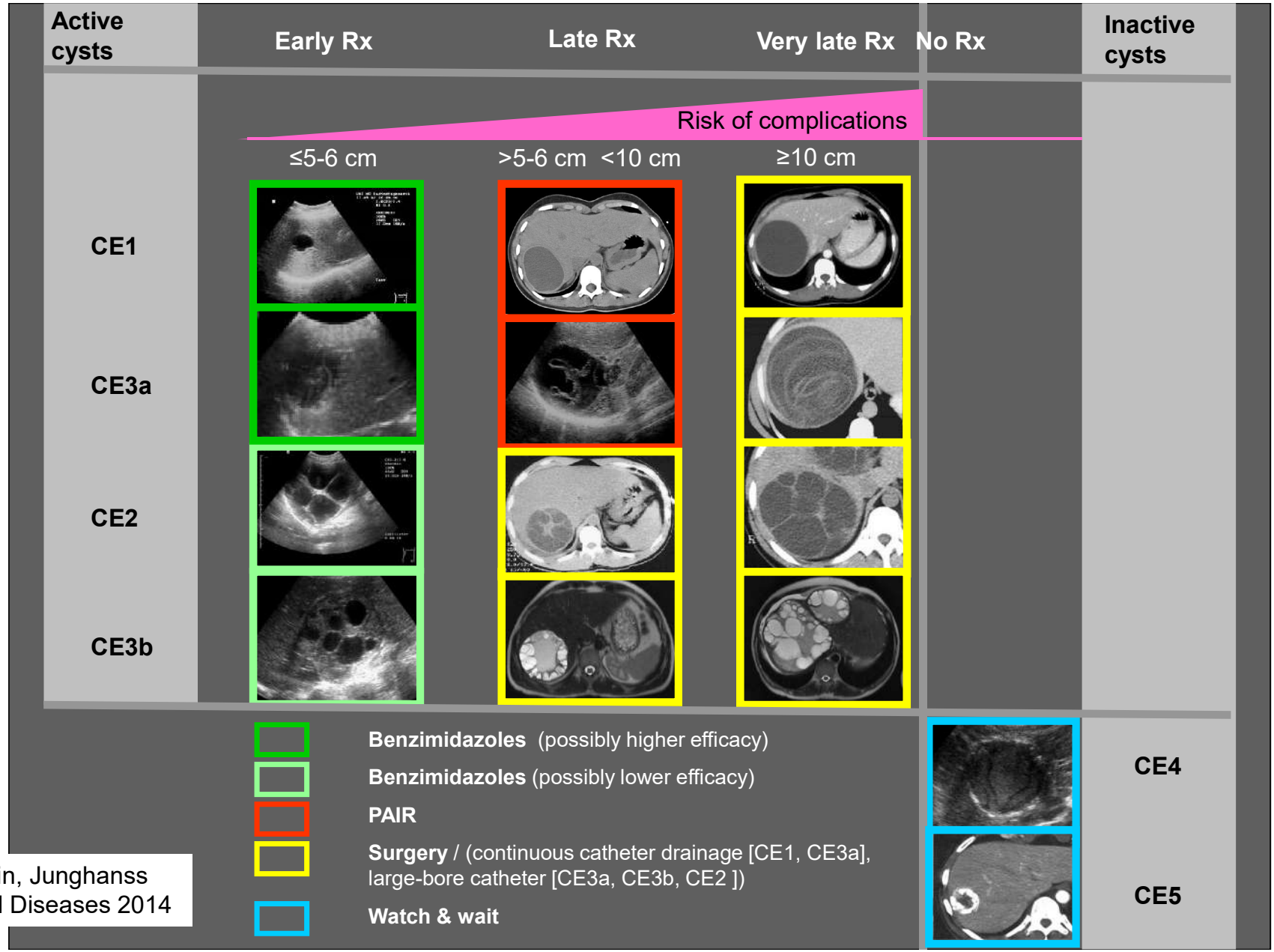
Images: Heidelberg University Hospital

Why staging?

The „dying“ parasite



Stage-specific treatment of *uncomplicated* cysts

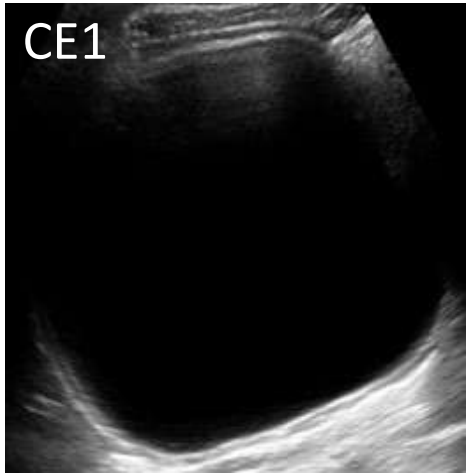


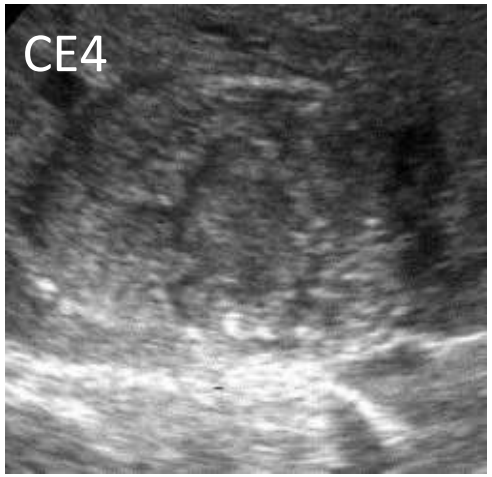
Stojkovic, Gottstein, Junghanss
Manson's Tropical Diseases 2014

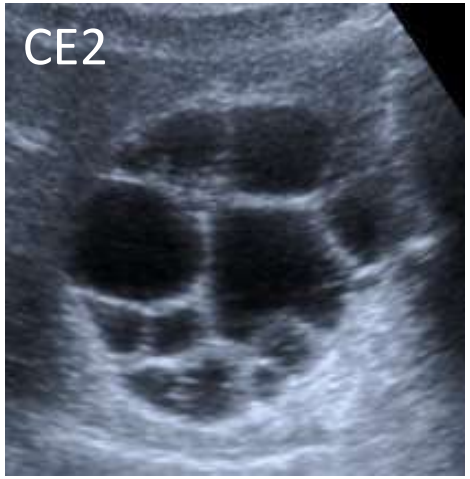
US-based imaging is the key to

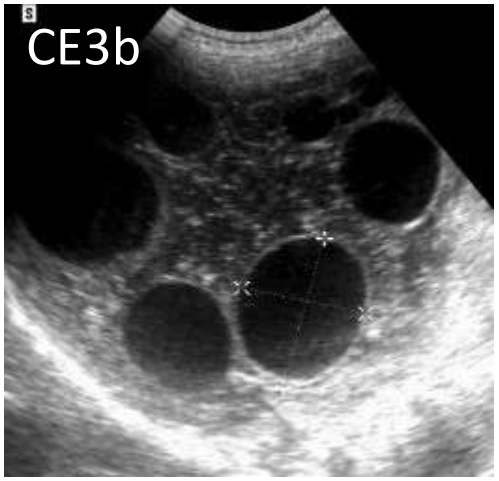
- Diagnosis
- Staging-based treatment decision
- Follow-up

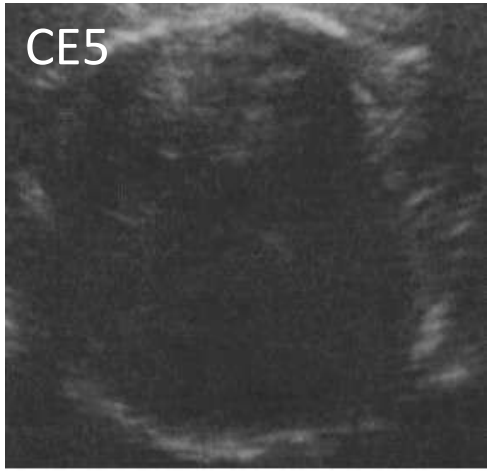
Diagnosis of CE .... there are a few tricky DDs!!







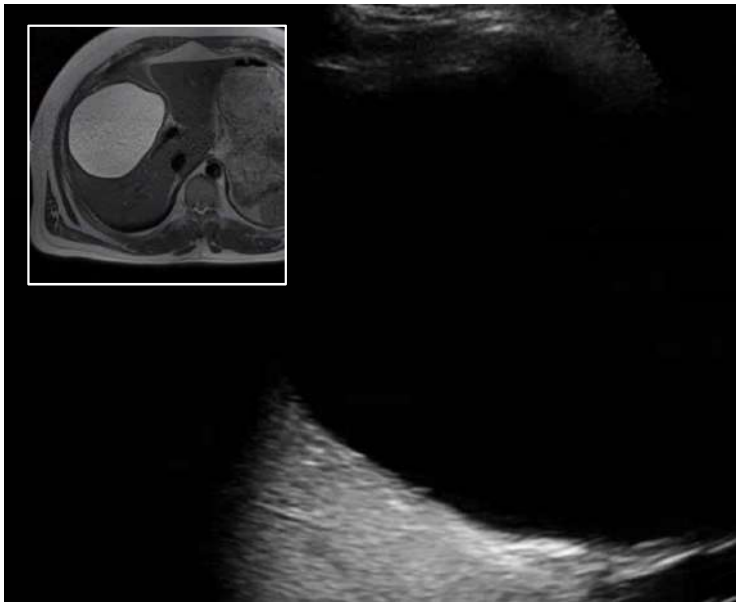




CE1
Double wall sign
CE2
Honeycomb appearance
CE3a
water lily sign
CE3b
Swiss cheese appearance
CE4
Ball of wool or canalicular or cerebroid appearance
CE5
Ball of wool or canalicular or cerebroid appearance

Images: Heidelberg University Hospital

Non-specific



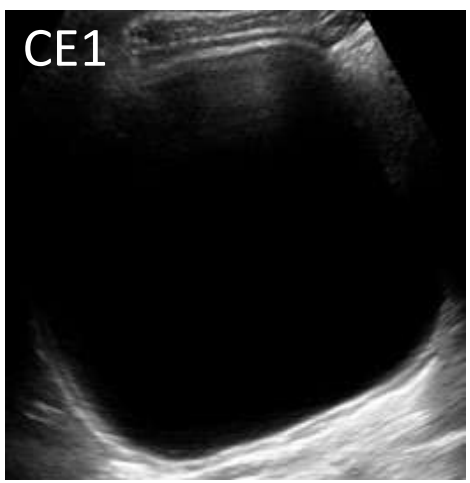
2269329

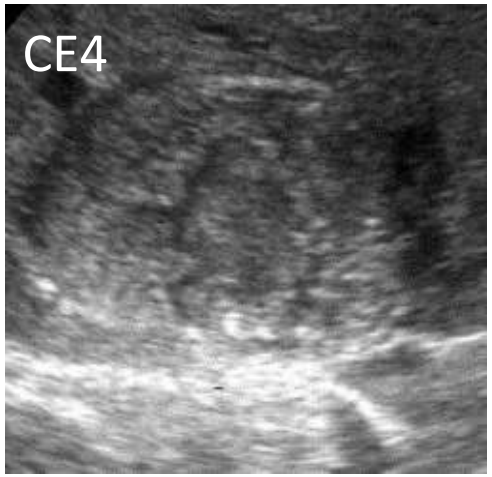
CE1

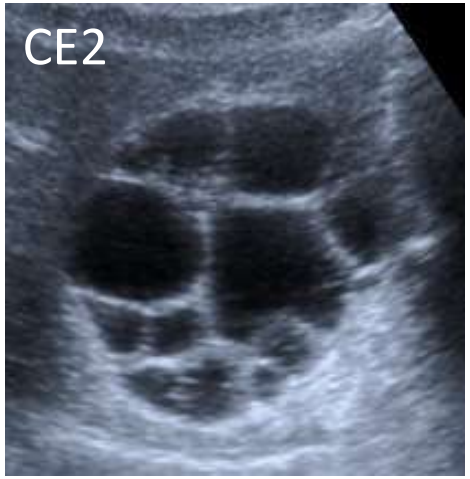
2332627

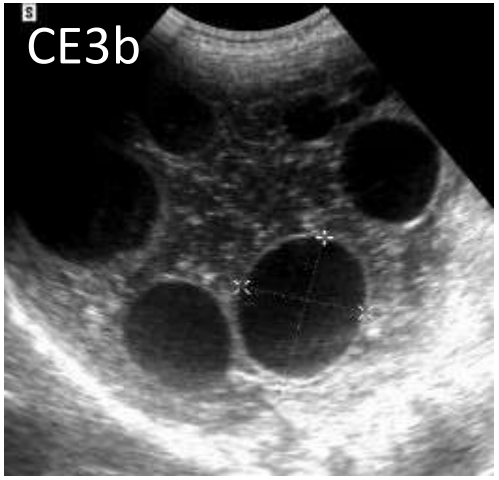
Double wall sign

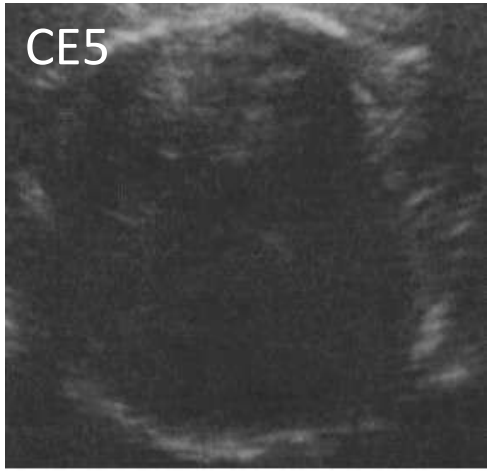
Staging of CE











CE1
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CE4
Ball of wool or canalicular or cerebroid
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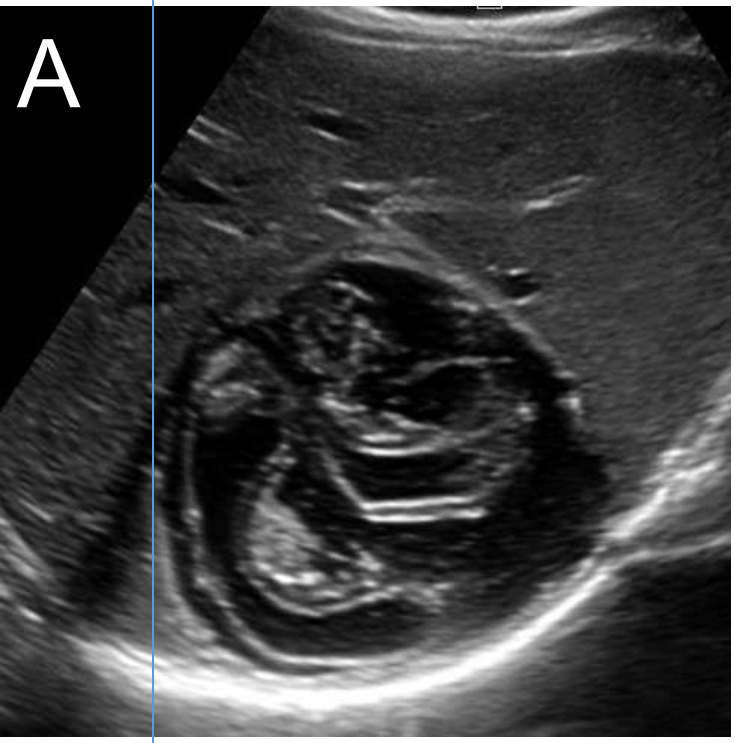
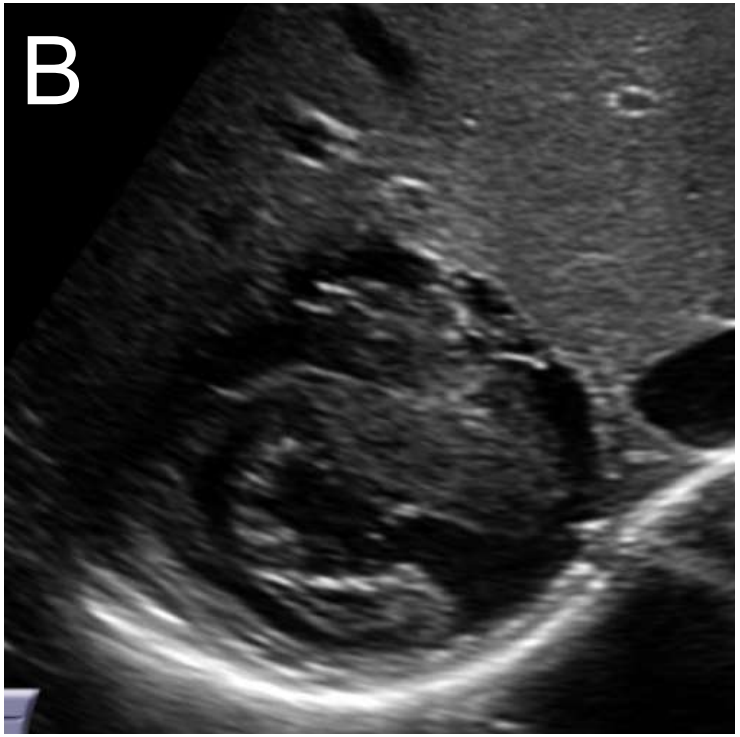
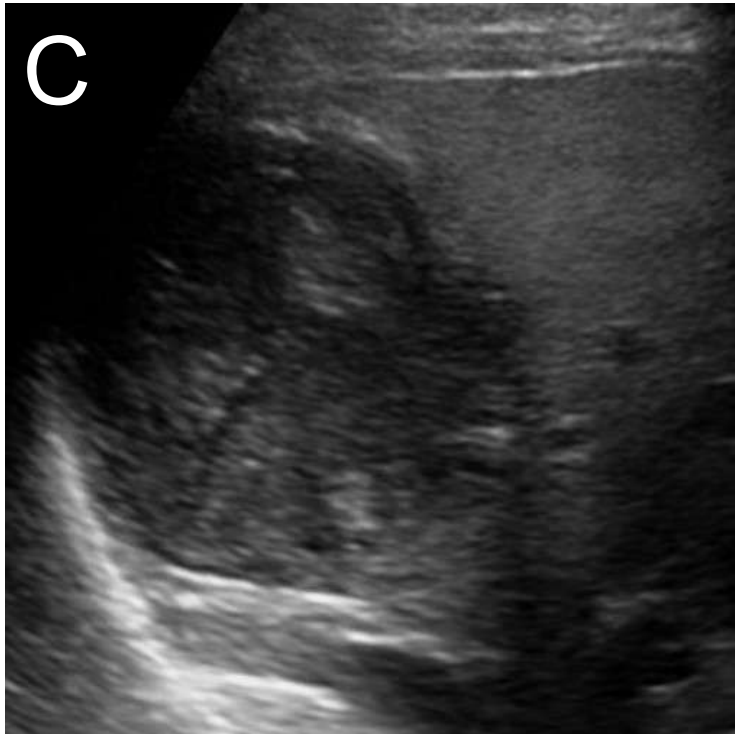
Ball of wool or canalicular or cerebroid appearance

Images: Heidelberg University Hospital

6 months ABZ







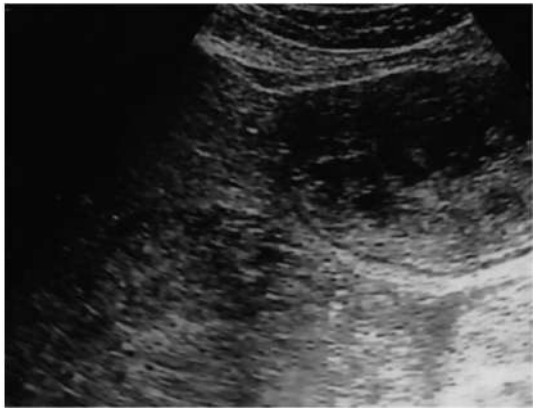
9 months

6 months

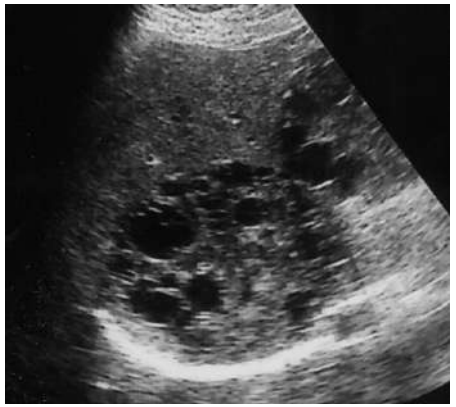
Heidelberg University Hospital

Relapsing CE 3b cysts

ABZ



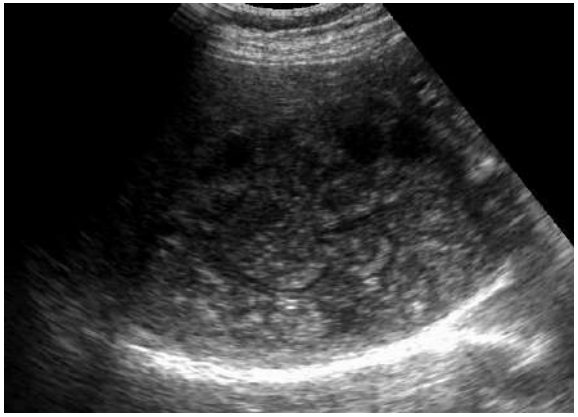
12 months



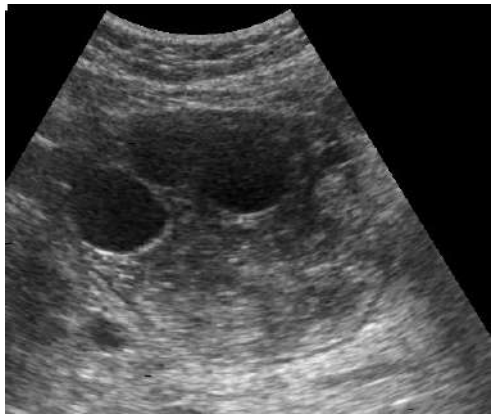
18 months

ABZ

12



months



14 months

Images: Heidelberg University Hospital

What to do when CE cysts are not (well) accessible with US?

- CE-cysts of the abdominal organs in adipose patients
- CE-cysts of the lung
- CE-cysts in other organs


10cm
V 120
ff.mAs 165
10mm
120
260
0.75
RAD.GE
Images: Heidelberg University Hospital

Translating US-based CE cysts cassification into other imaging modalities

- CT
- MRI

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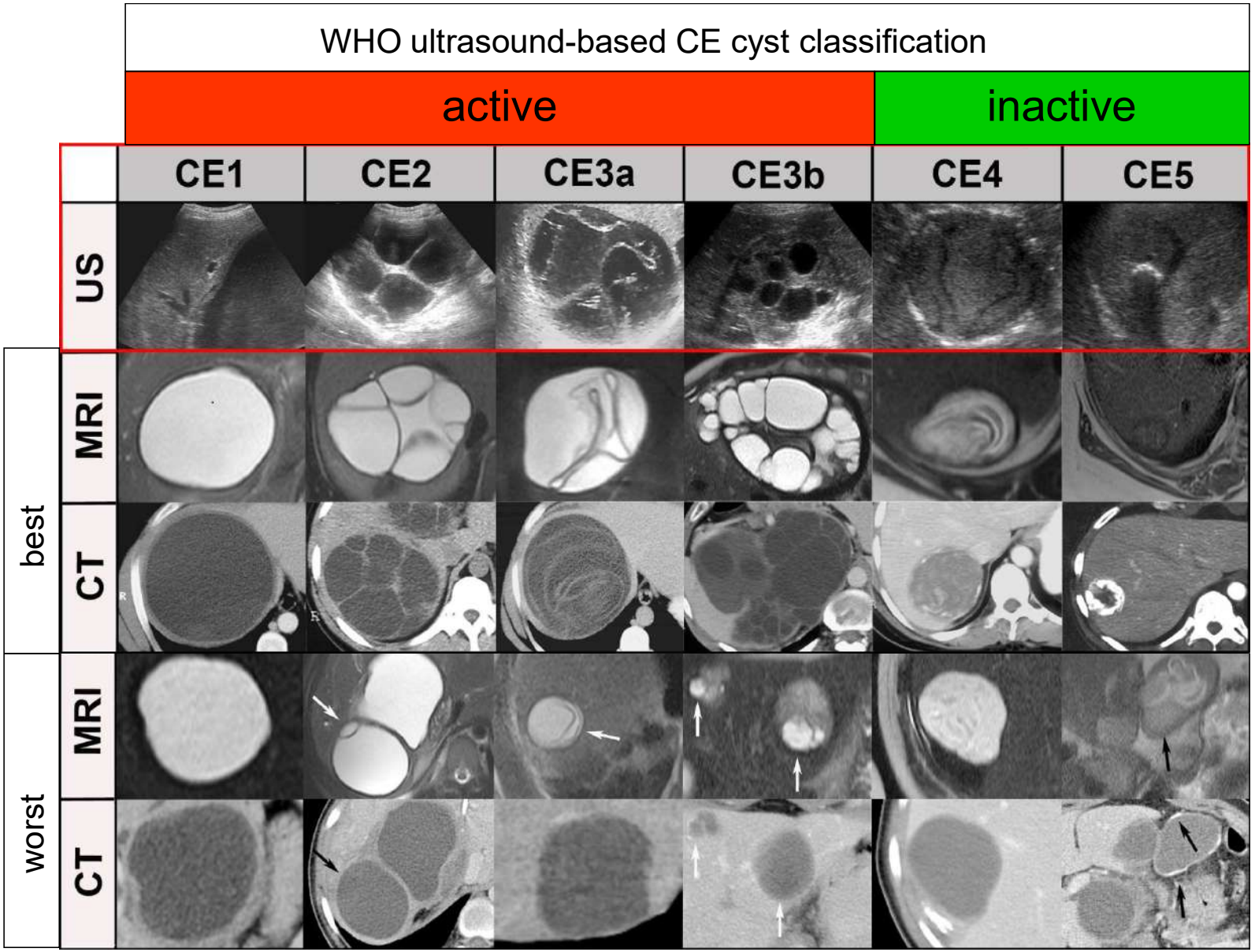
PLOS | NEGLECTED TROPICAL DISEASES

Diagnosing and Staging of Cystic Echinococcosis: How Do CT and MRI Perform in Comparison to Ultrasound?

Marija Stojkovic[1], Kerstin Rosenberger[1], Hans-Ullrich Kauczor[2], Thomas Junghanss[1]*, Waldemar Hosch[2]

1 Section Clinical Tropical Medicine, Department of Infectious Diseases, Heidelberg University Hospital, Heidelberg, Germany, **2** Department of Diagnostic and Interventional Radiology, Heidelberg University Hospital, Heidelberg, Germany



Stojkovic et al (2012) PloS Negl Trop Dis 6(10)

Scatter plot of the WHO classification-based cyst staging with a level of agreement beyond chance of the individual CE stages

κ CE 1–4 cysts

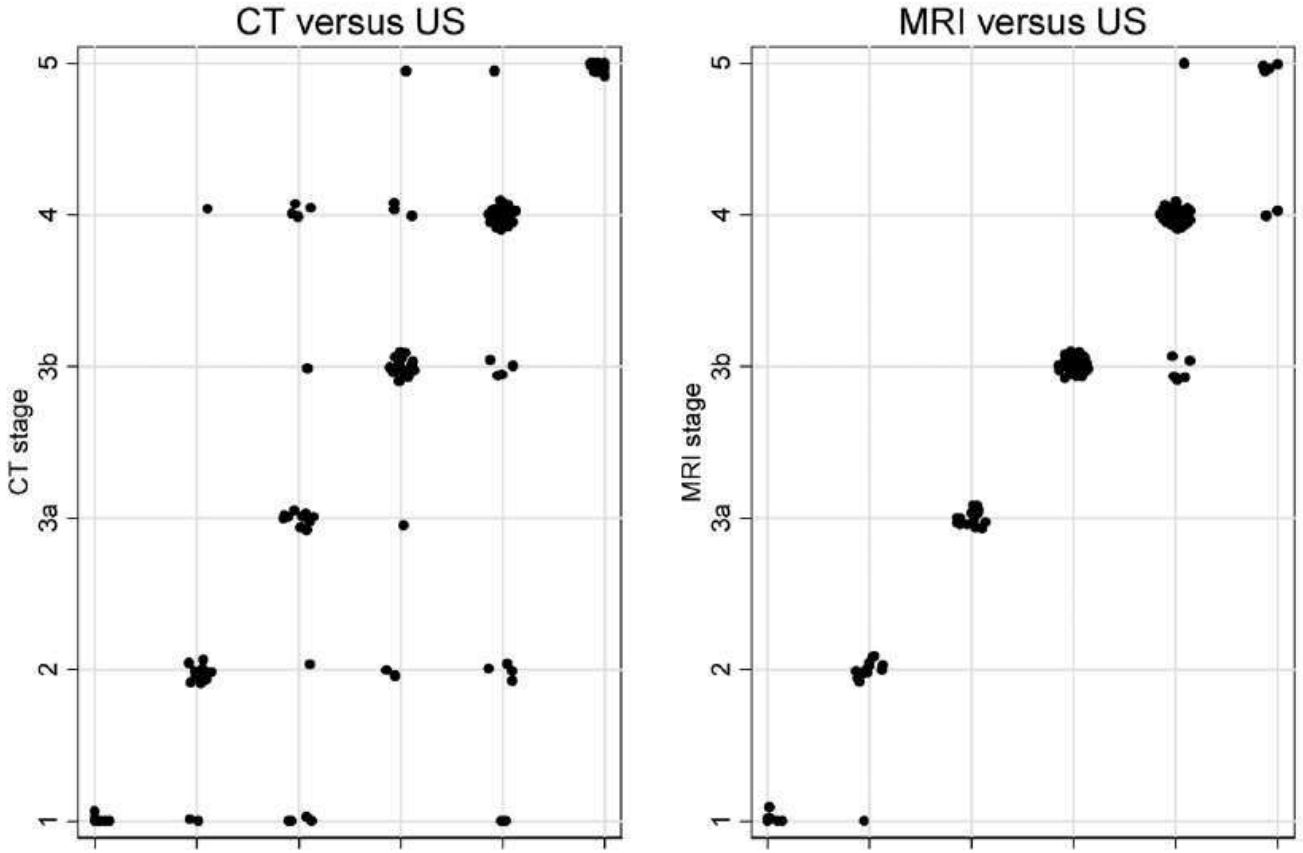
MRI 0.83 to 1.0

CT 0.62 to 0.72

κ CE5 cysts

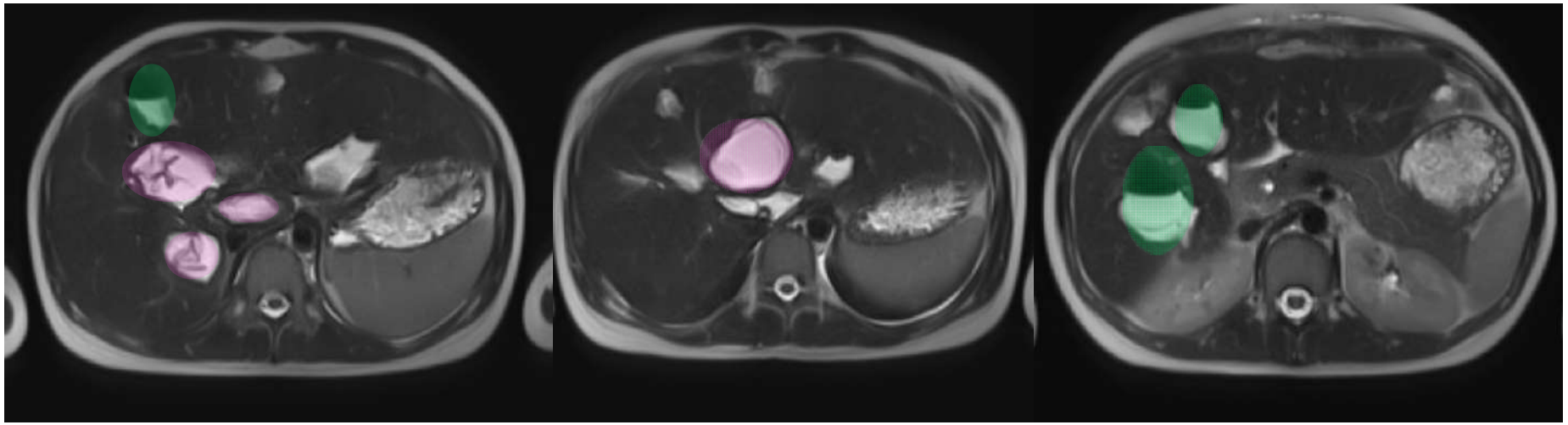
CT 0.95

MRI 0.65



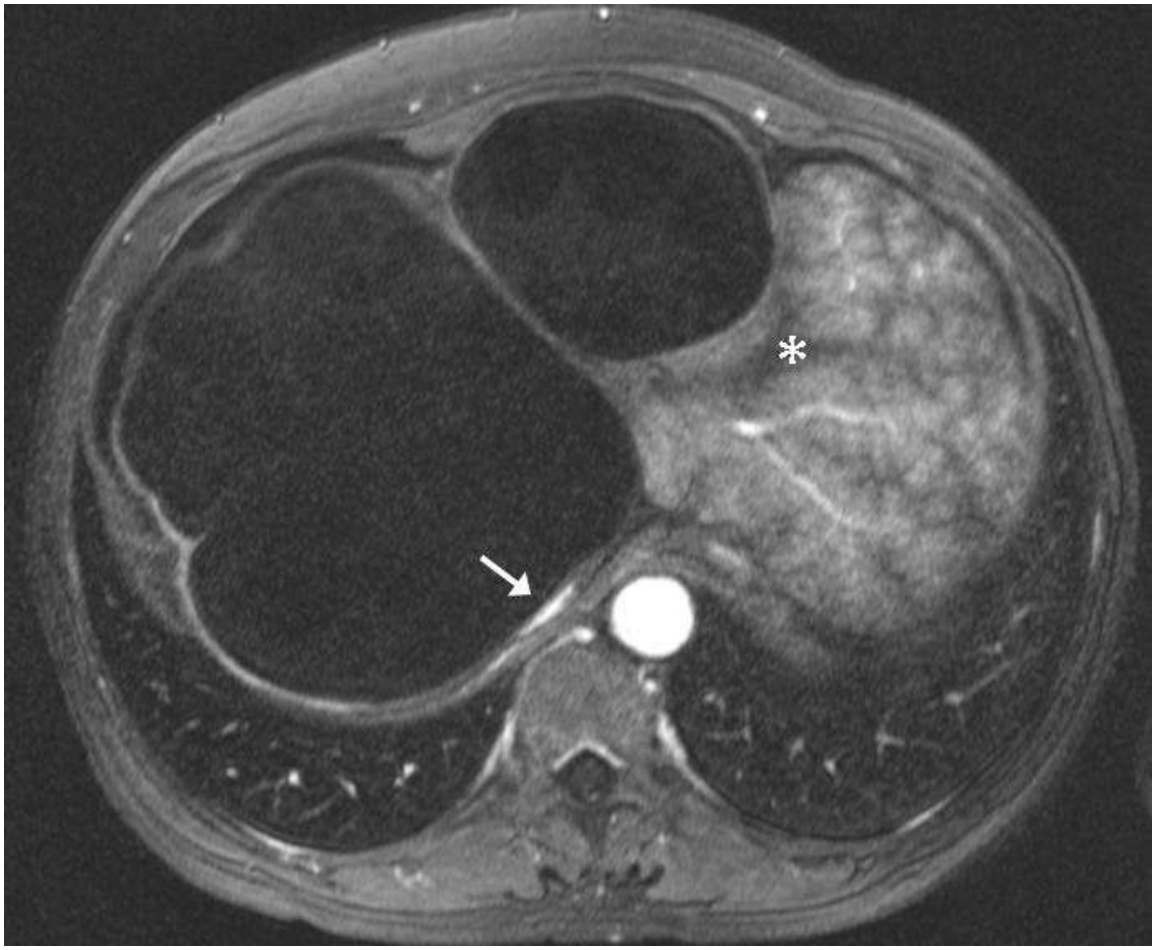
Stojkovic et al (2012) PloS Negl Trop Dis 6(10)

Liver

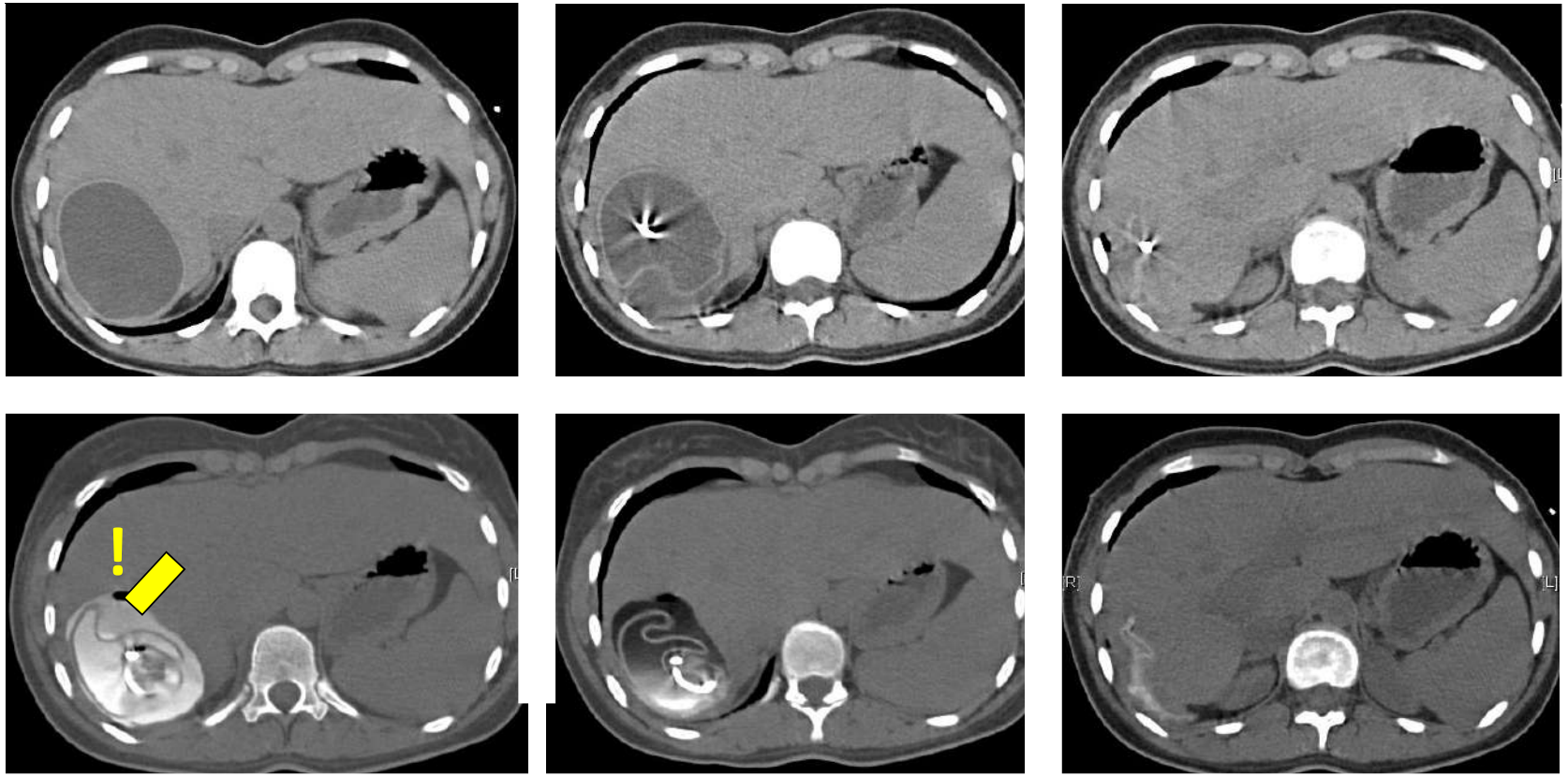


Images: Heidelberg University Hospital

Budd-Chiari Syndrome



Images: Heidelberg University Hospital



PAIR

Images: Heidelberg University Hospital

ELSEVIER

European Journal of Radiology 66 (2008) 262–267

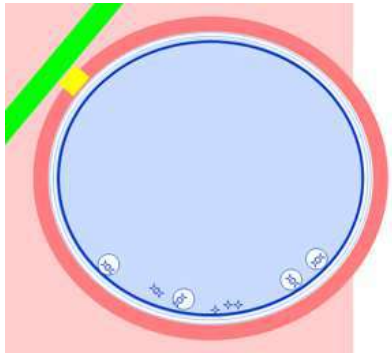
EJR
EUROPEAN JOURNAL OF RADIOLOGY

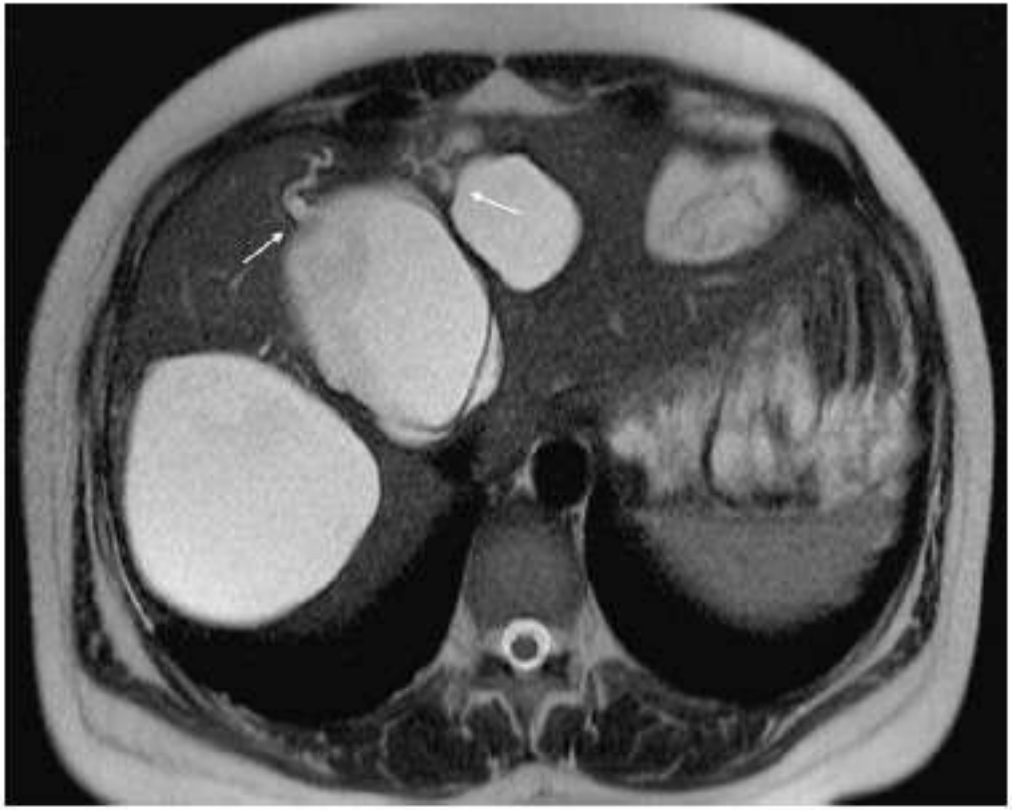
www.elsevier.com/locate/ejrad

MR imaging for diagnosing cysto-biliary fistulas in cystic echinococcosis

Waldemar Hosch [a,*], Marija Stojkovic [b], Thomas Jänisch [c], Tobias Heye [a], Jens Werner [d], Helmut Friess [d], Günter W. Kauffmann [a], Thomas Junghanss [b]

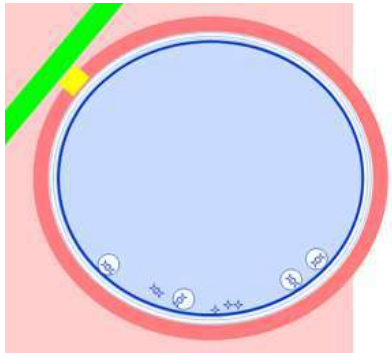
[a] *Department of Radiology, University Hospital of Heidelberg, Im Neuenheimer Feld 110, 69120 Heidelberg, Germany*
[b] *Section of Clinical Tropical Medicine, University Hospital of Heidelberg, Germany*
[c] *Section of Biostatistics and Epidemiology, University Hospital of Heidelberg, Germany*
[d] *Department of Surgery, University Hospital of Heidelberg, Germany*

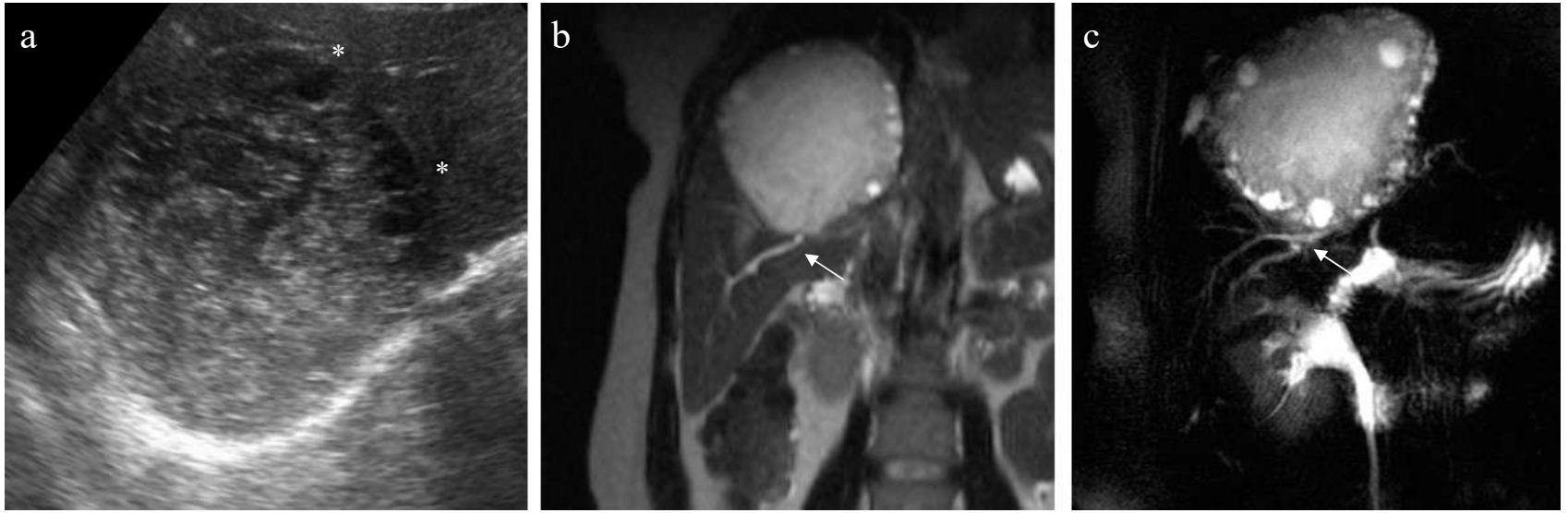




Transversal T2 Haste sequence

Hosch W, Stojkovic M, Jänisch T, Heye T, Werner J, Friess H, Kauffmann GW, Junghanss T
MR imaging for diagnosing cysto-biliary fistulas in cystic echinococcosis.
Eur J Radiol. 2008 May; 66 (2):262-7.



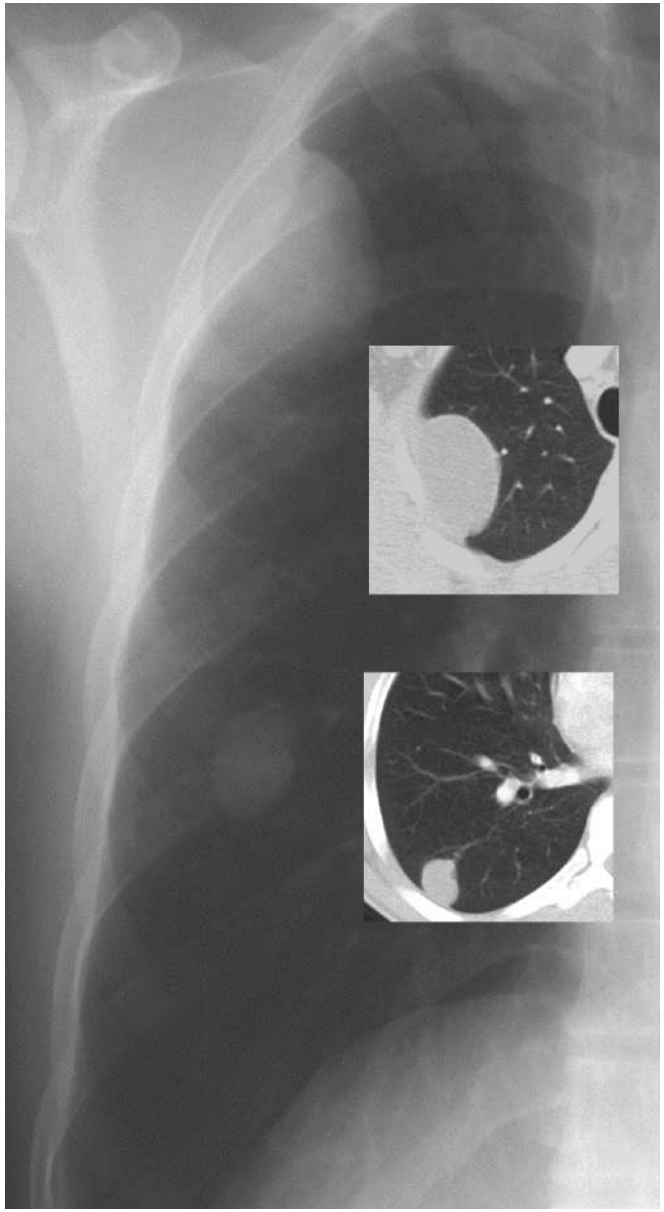


a. US imaging: WHO CE 3b cyst with solid content and multiple daughter cysts along the periphery

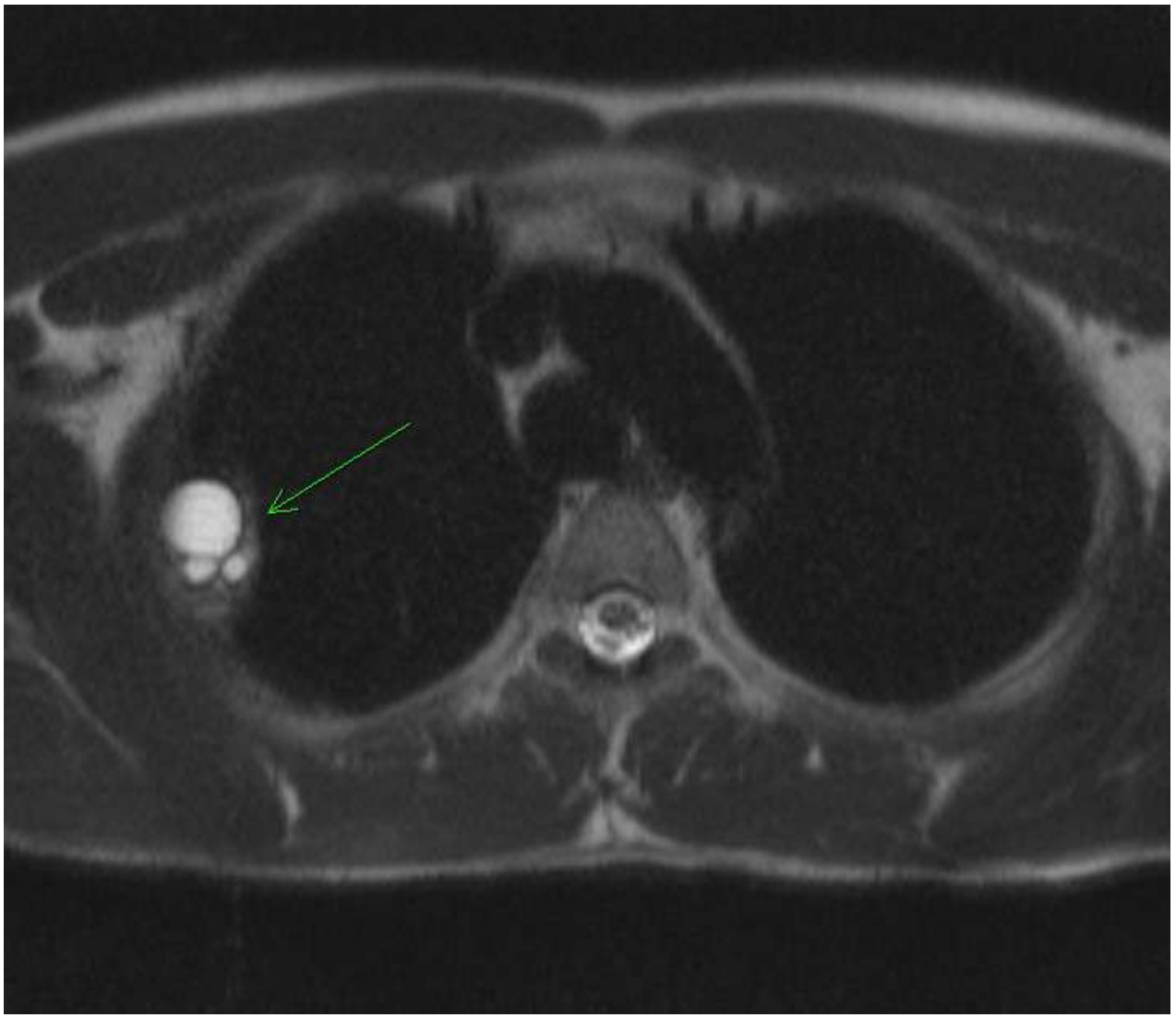
MR imaging: T2-w TSE sequence (b) and T2-w RARE sequence (c). Dilated segmental bile duct with a cysto-biliary fistula

Hosch W, Stojkovic M, Jänisch T, Heye T, Werner J, Friess H, Kauffmann GW, Junghanss T
MR imaging for diagnosing cysto-biliary fistulas in cystic echinococcosis.
Eur J Radiol. 2008 May; 66 (2):262-7.

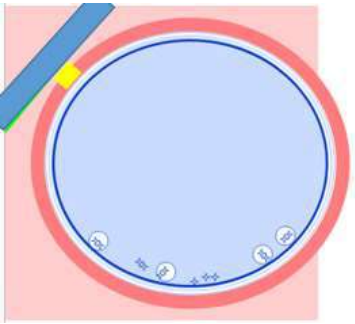
Lung

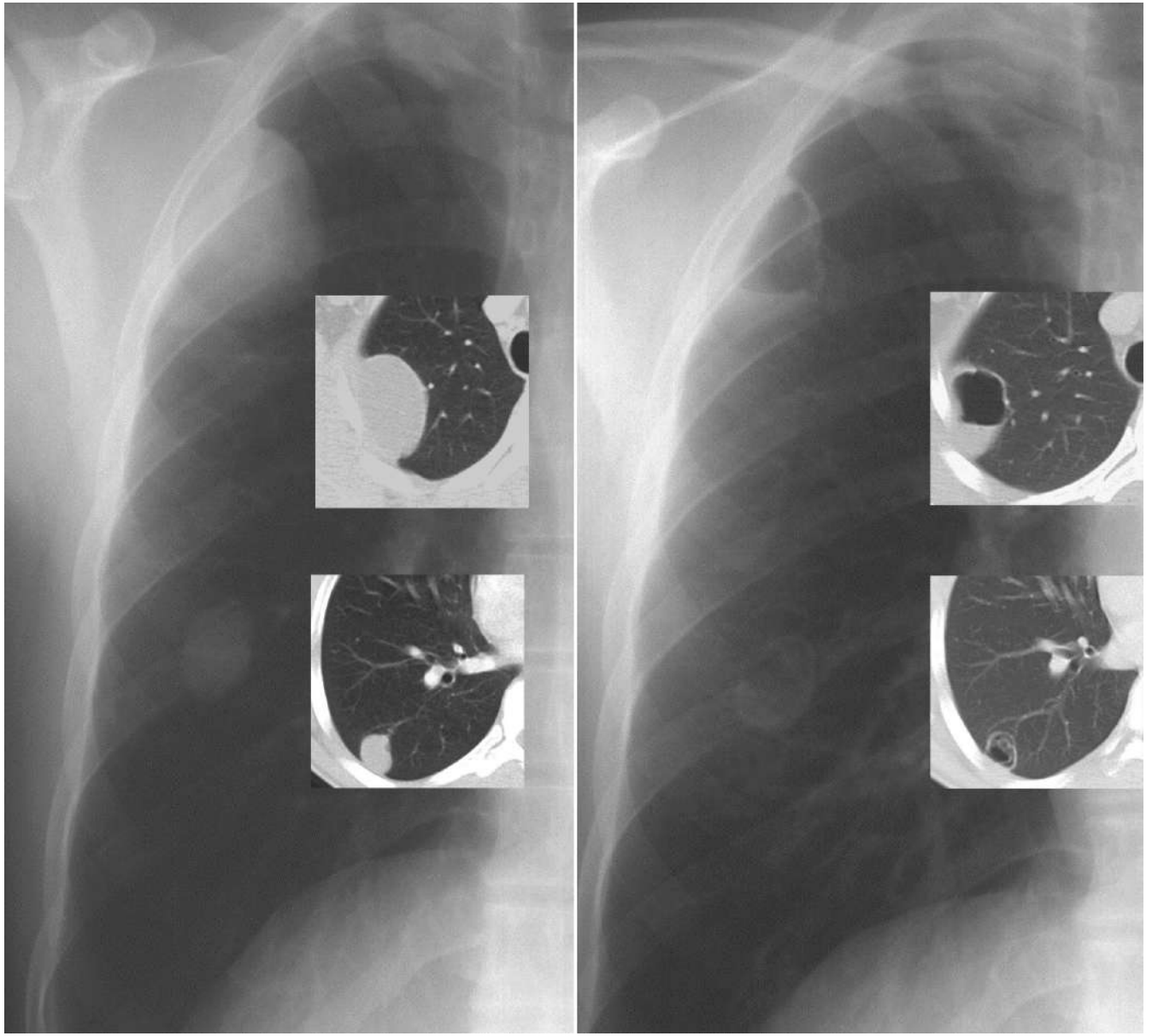


Heidelberg University Hospital



Heidelberg University Hospital





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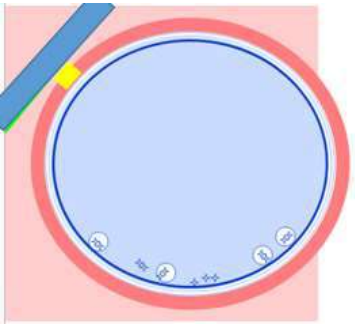
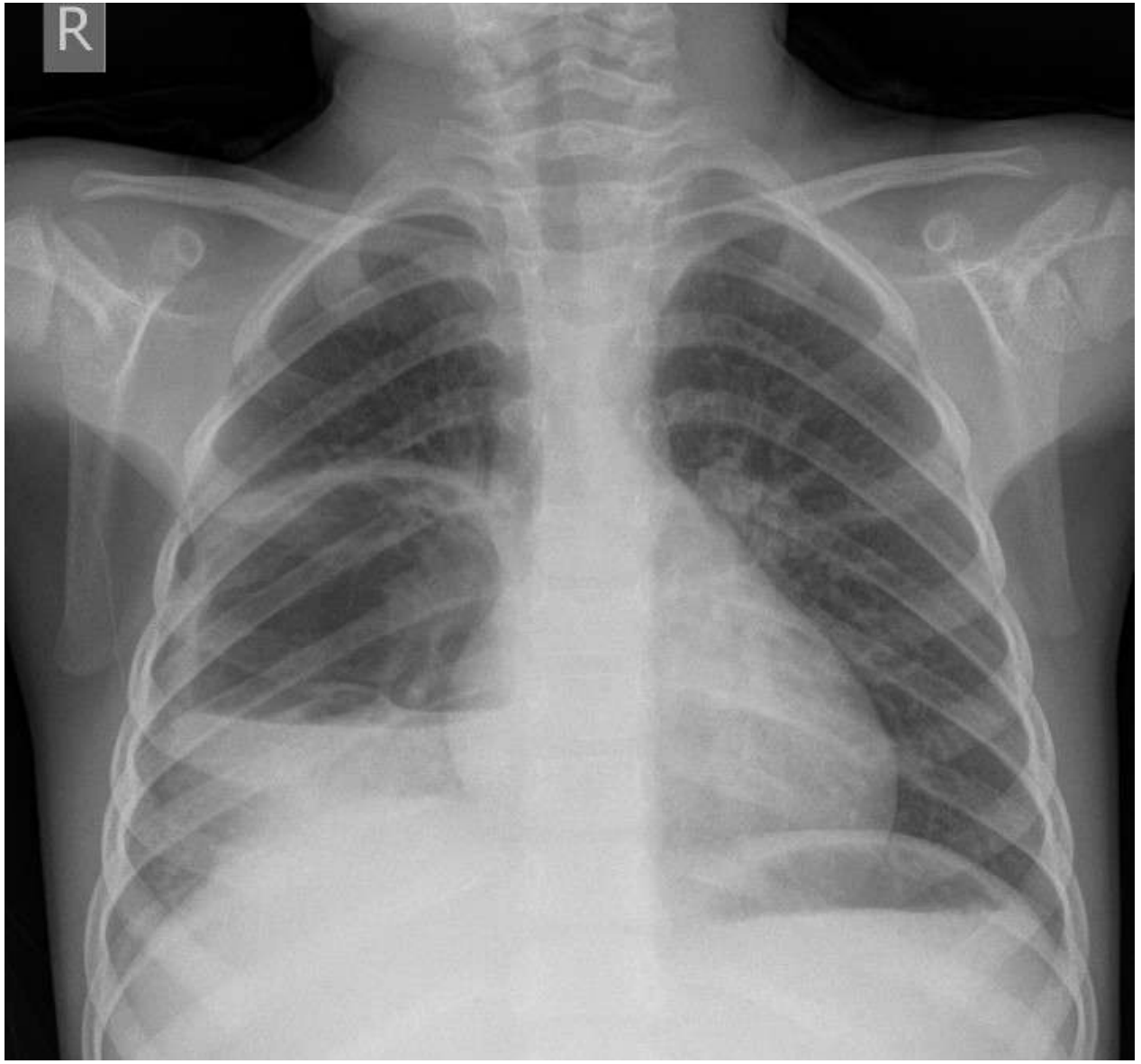
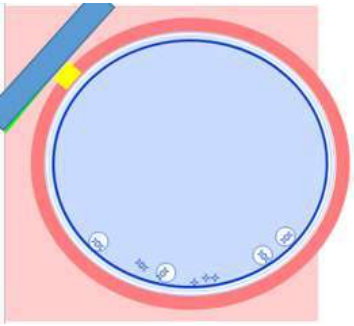
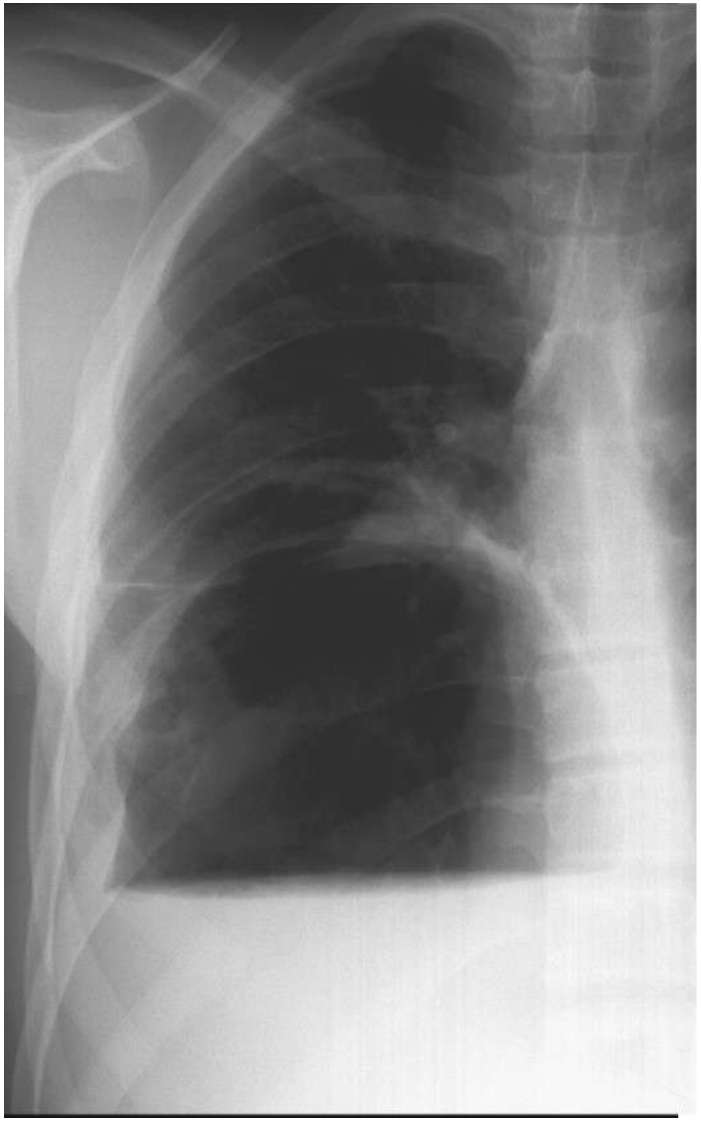
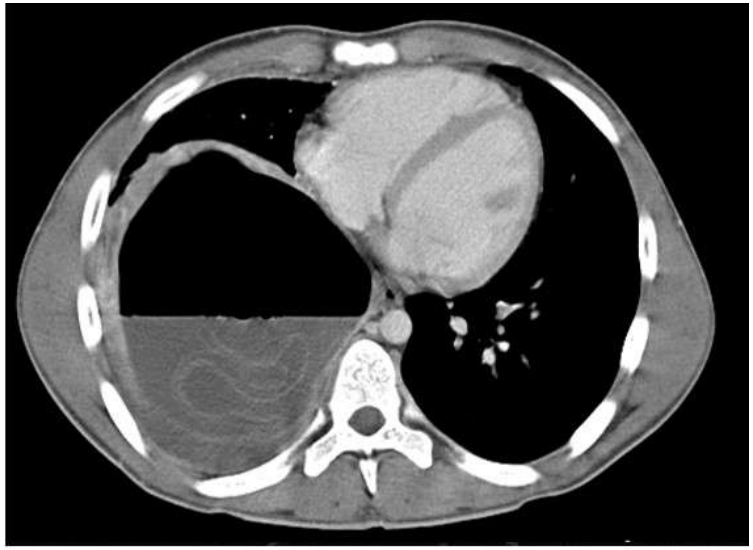


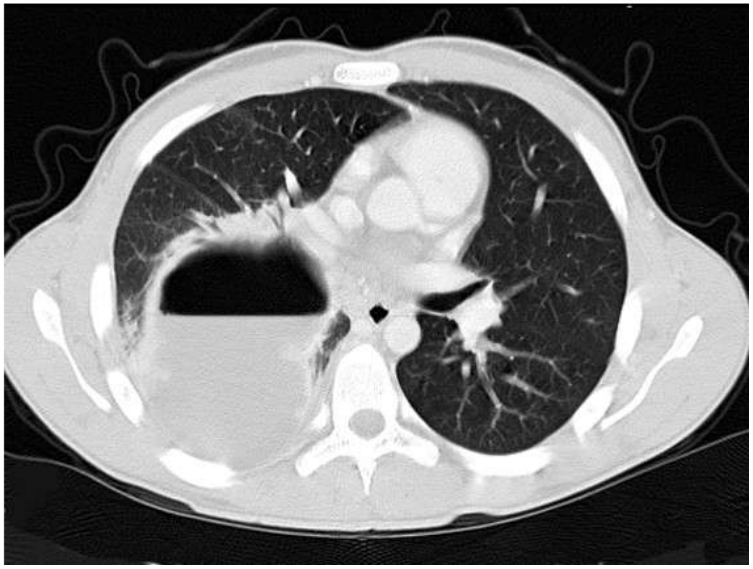


Heidelberg University Hospital









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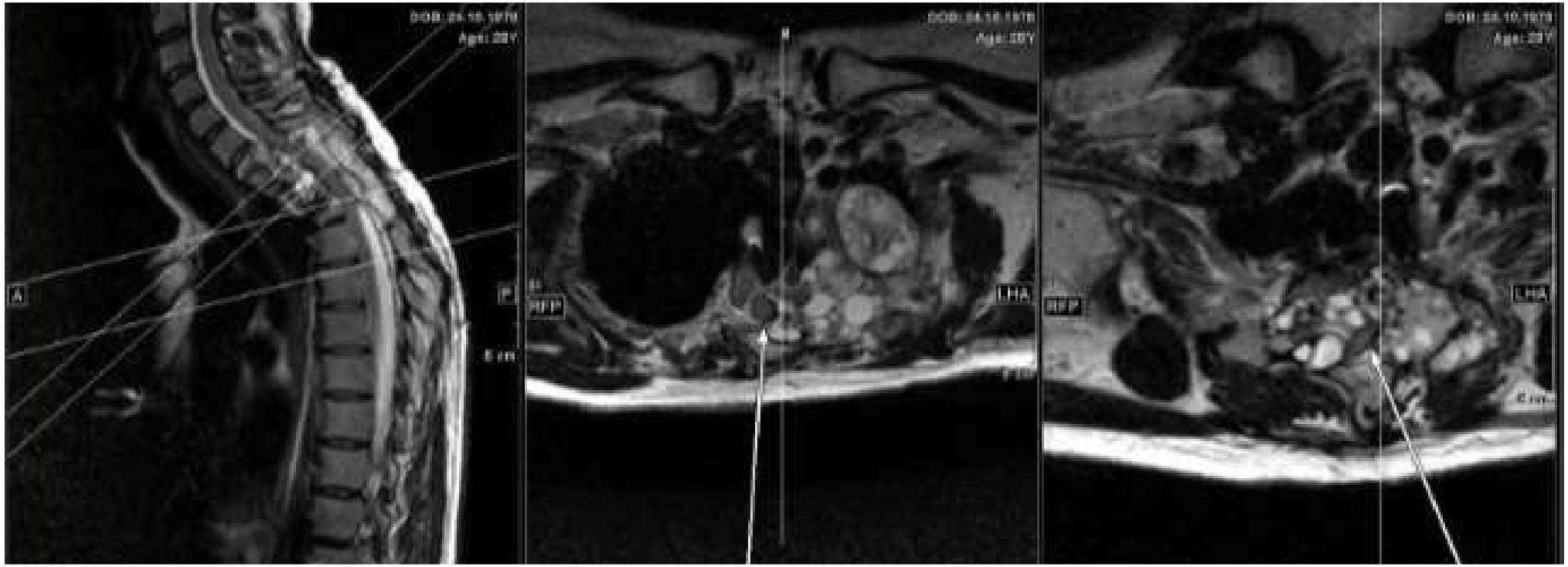
Other organs



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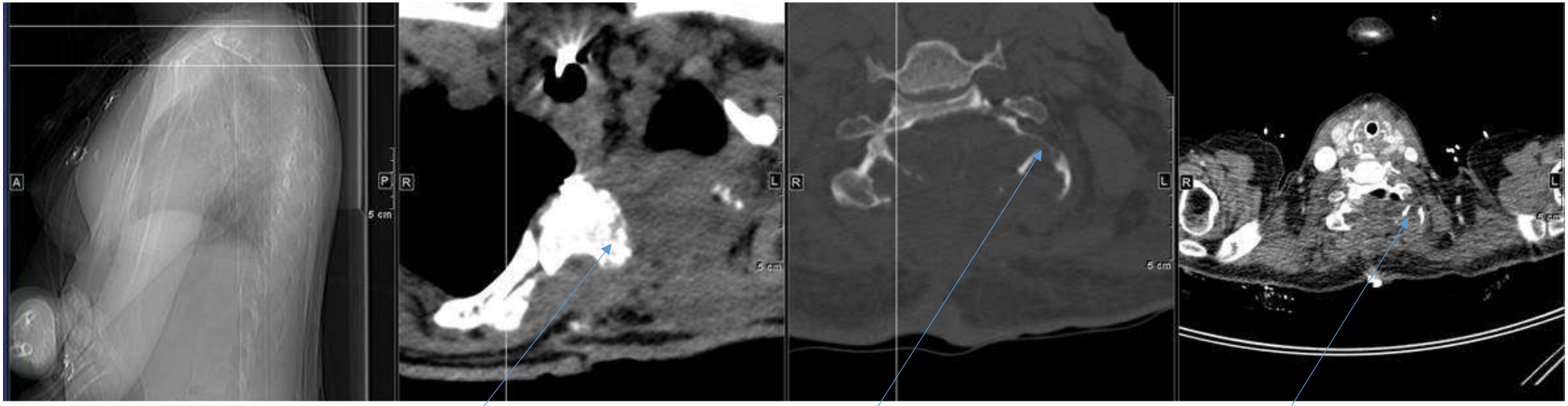
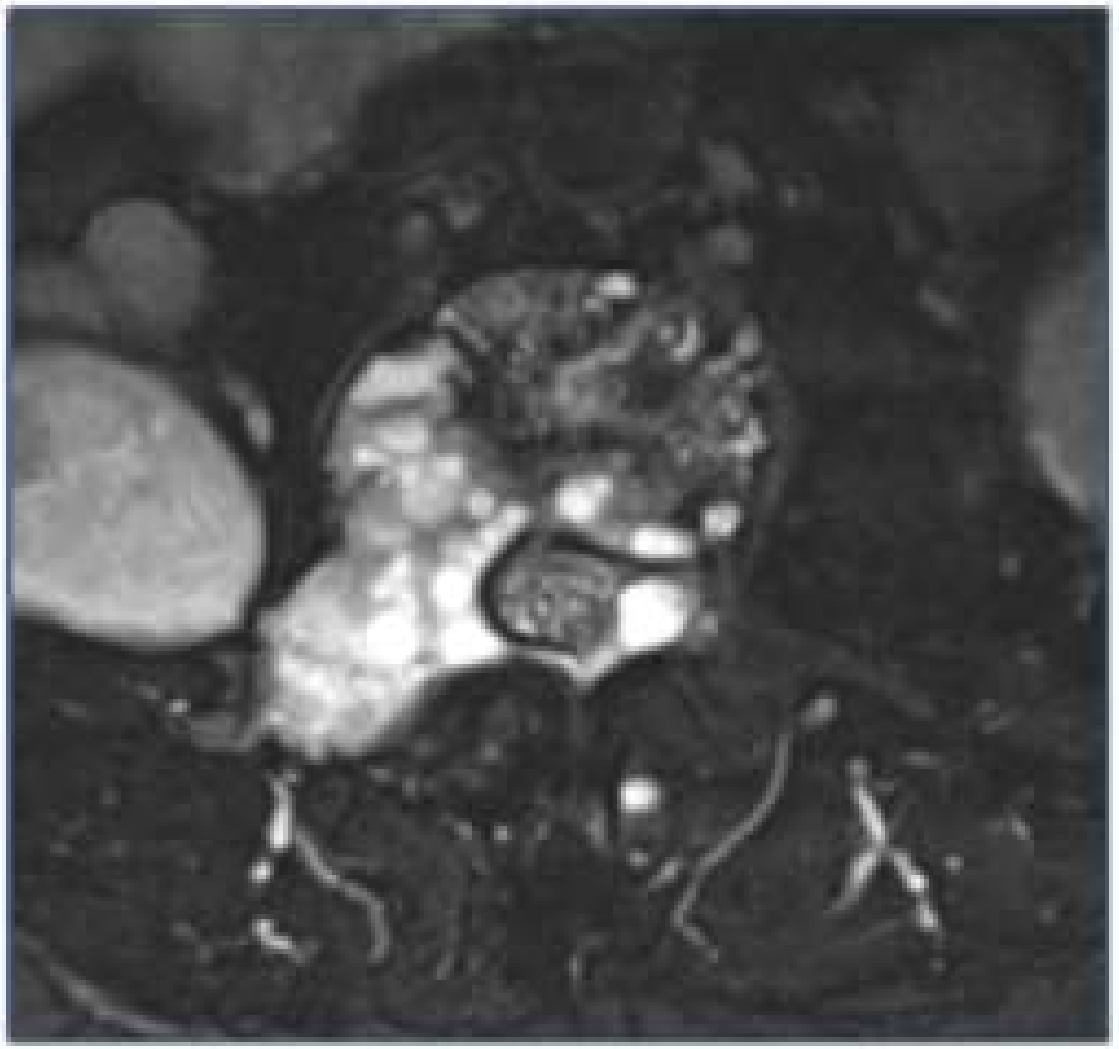


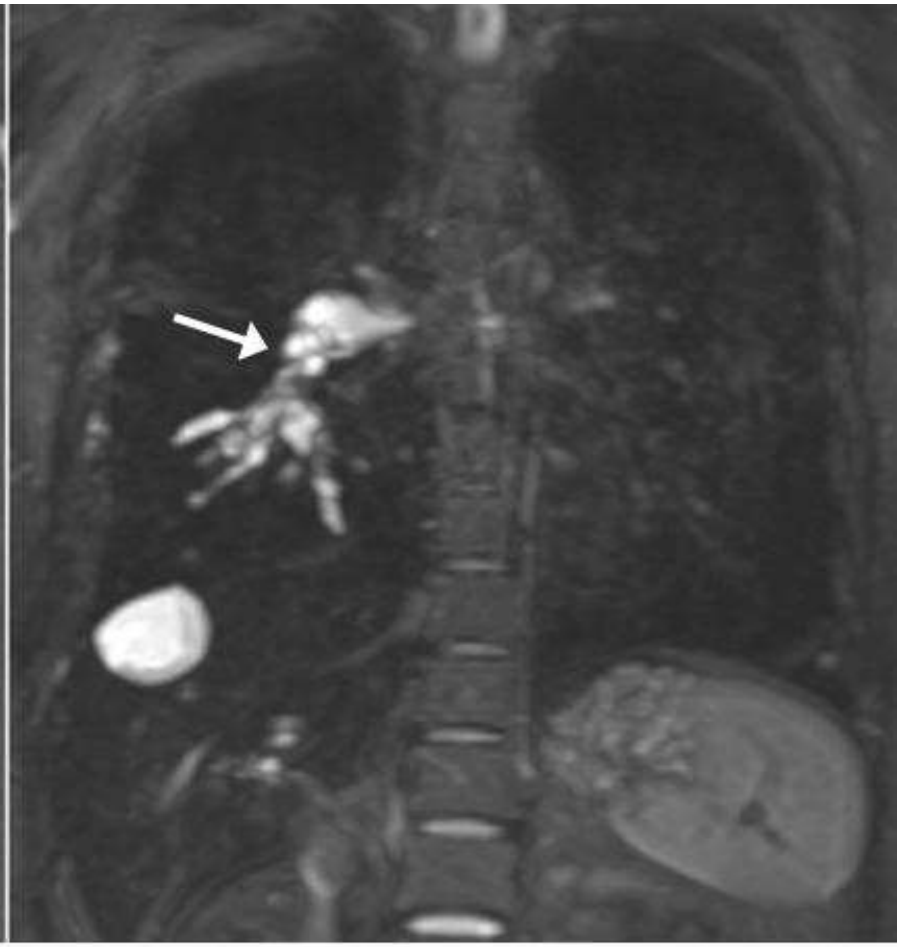
Infiltrative growth

Heidelberg University Hospital



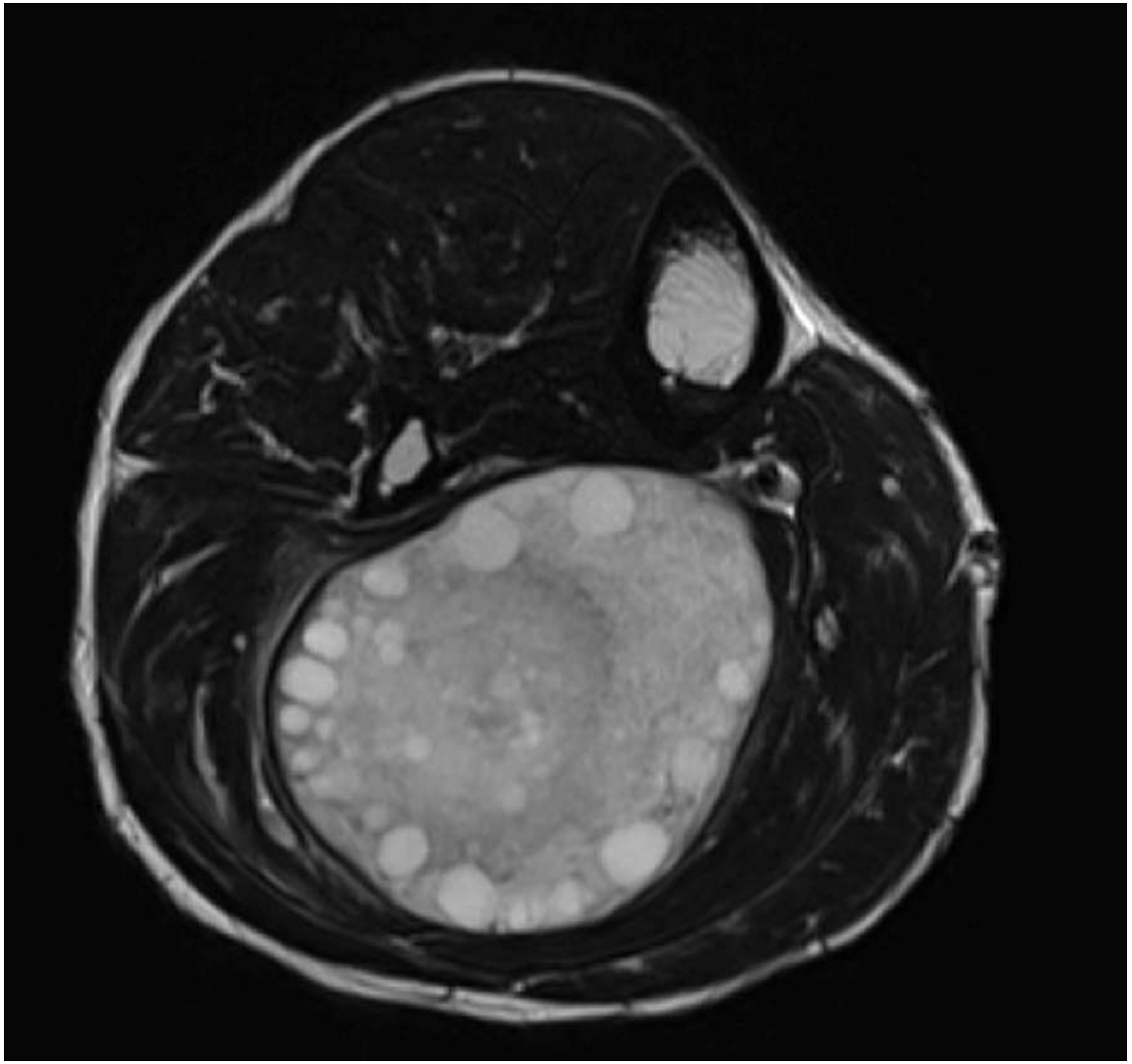
Heidelberg University Hospital

Perfusion defect of the right hemithorax

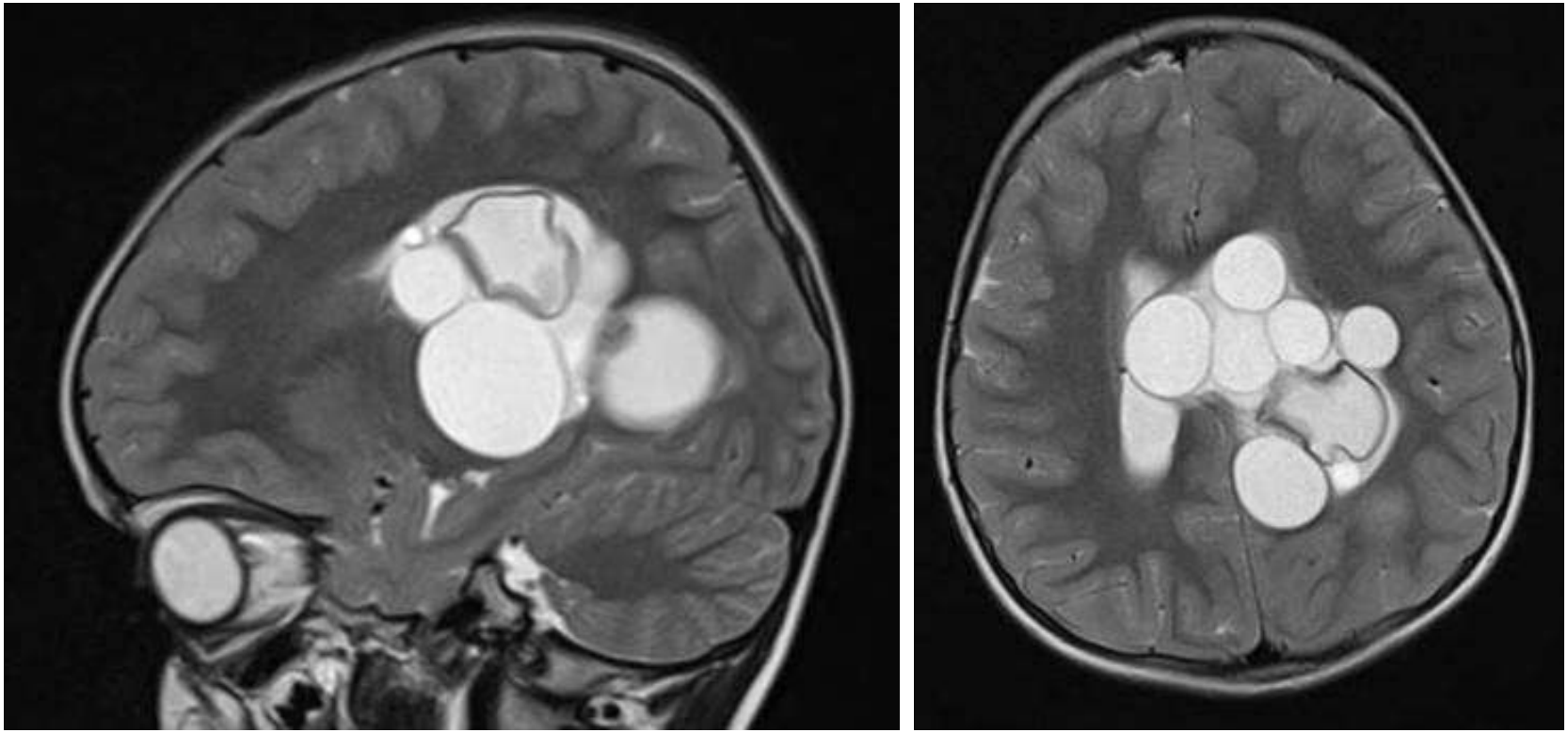


Central pulmonary embolism of the right pulmonary artery

Images: Heidelberg University Hospital

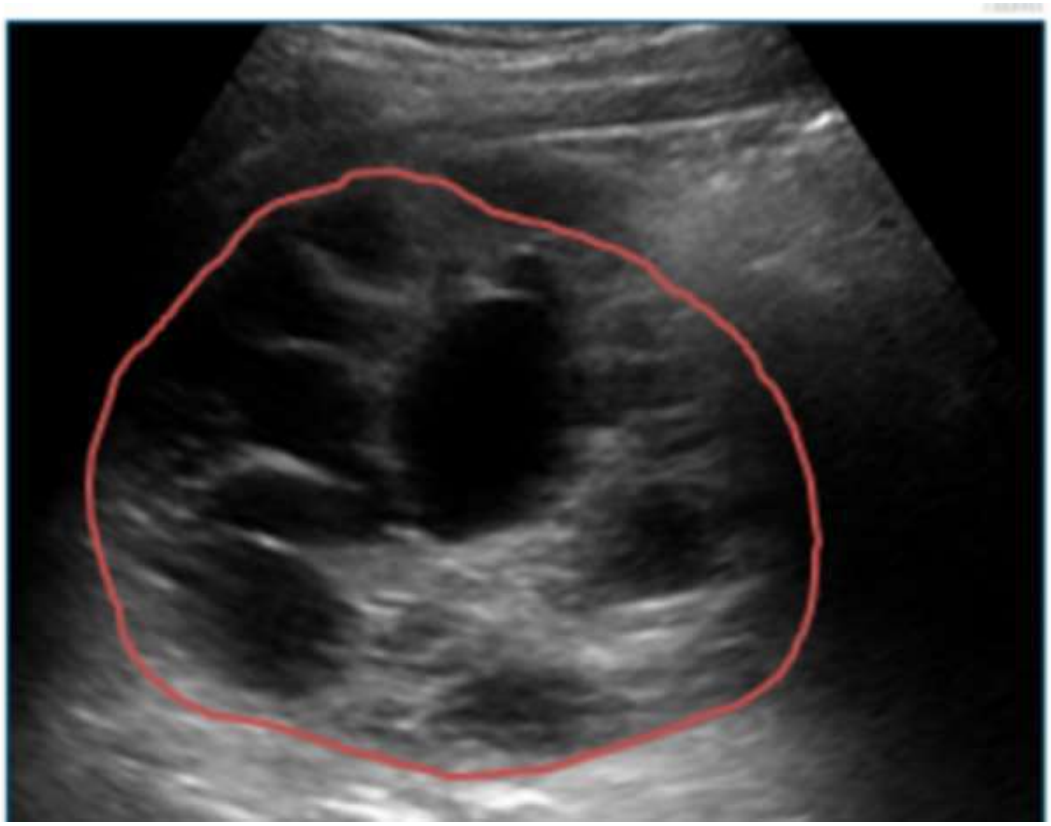


Heidelberg University Hospital



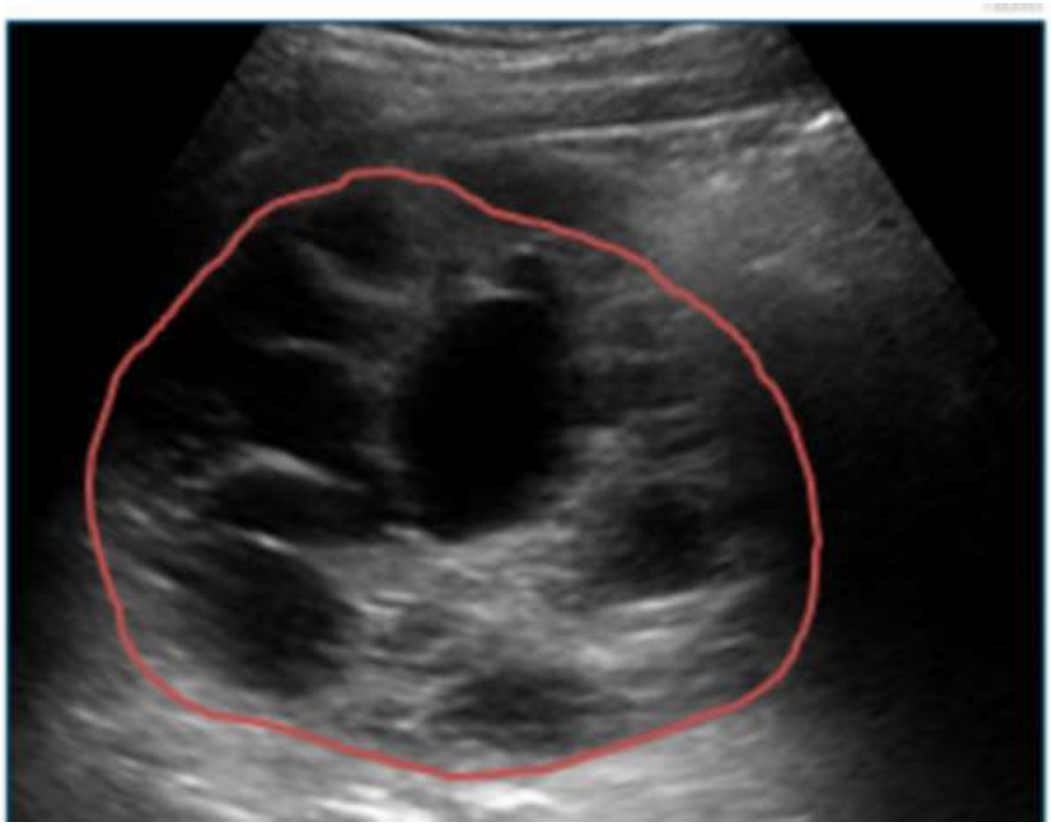
Images: Heidelberg University Hospital

Differential diagnosis



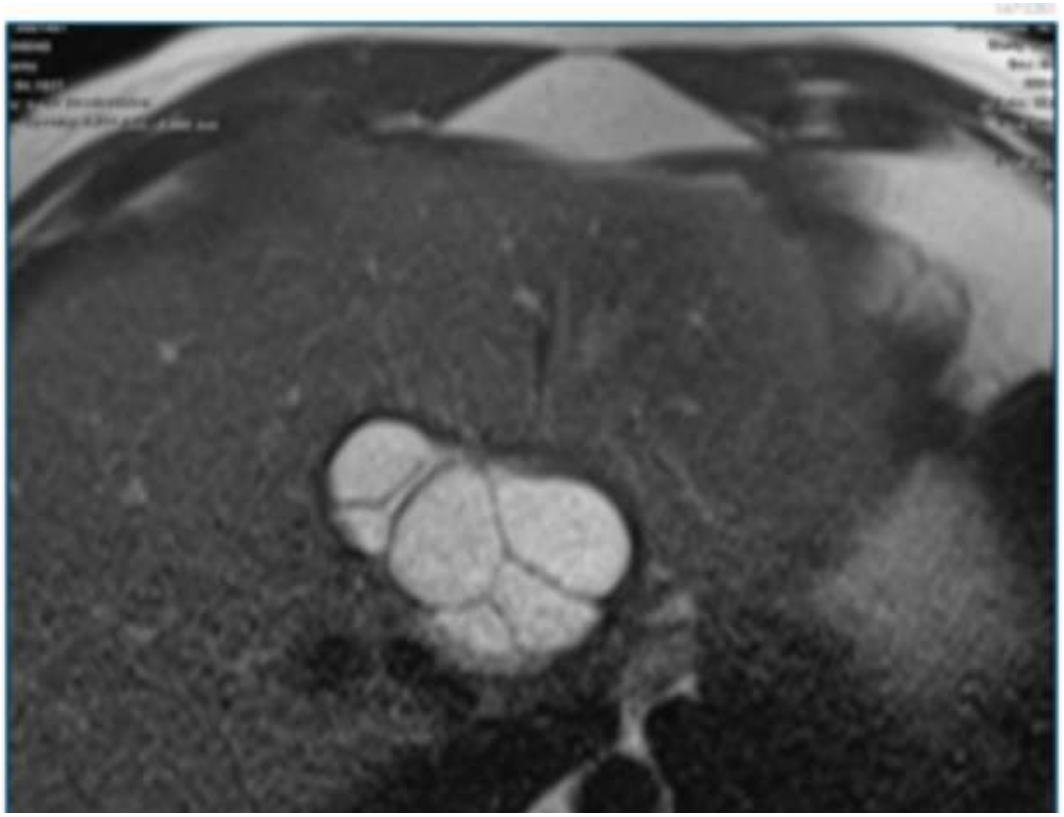
Heidelberg University Hospital

NET metastasis



CE 3b

Heidelberg University Hospital



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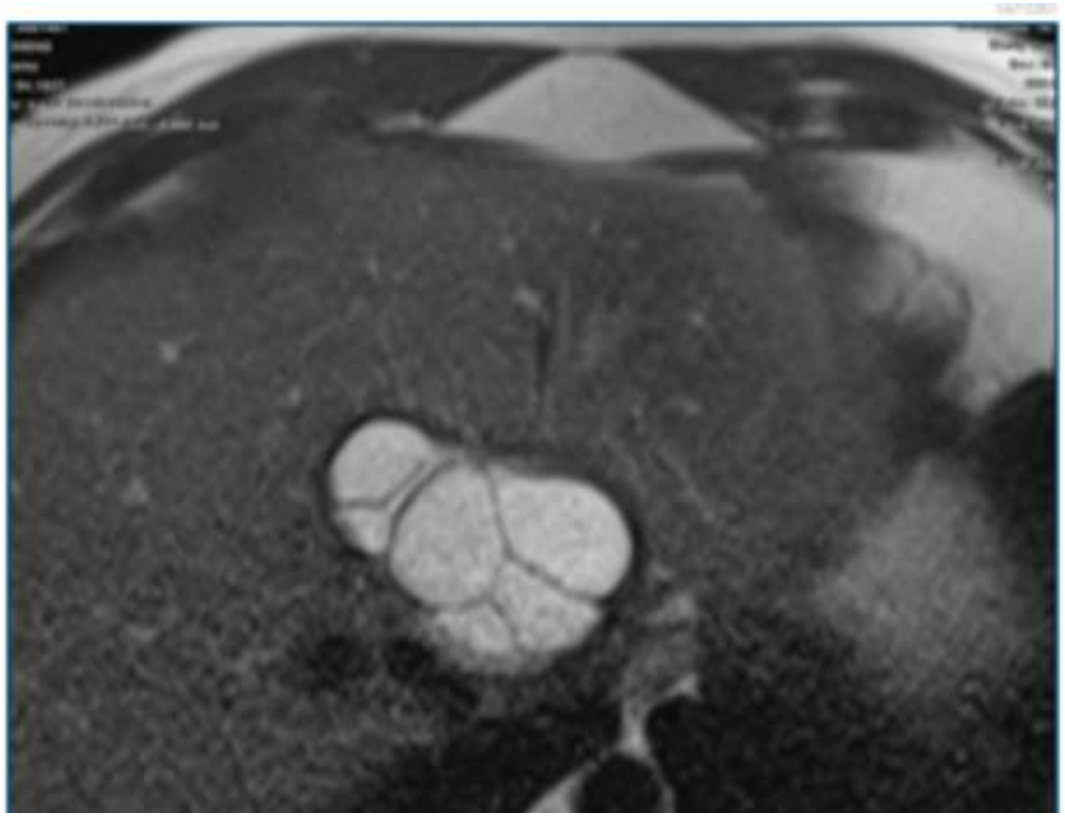
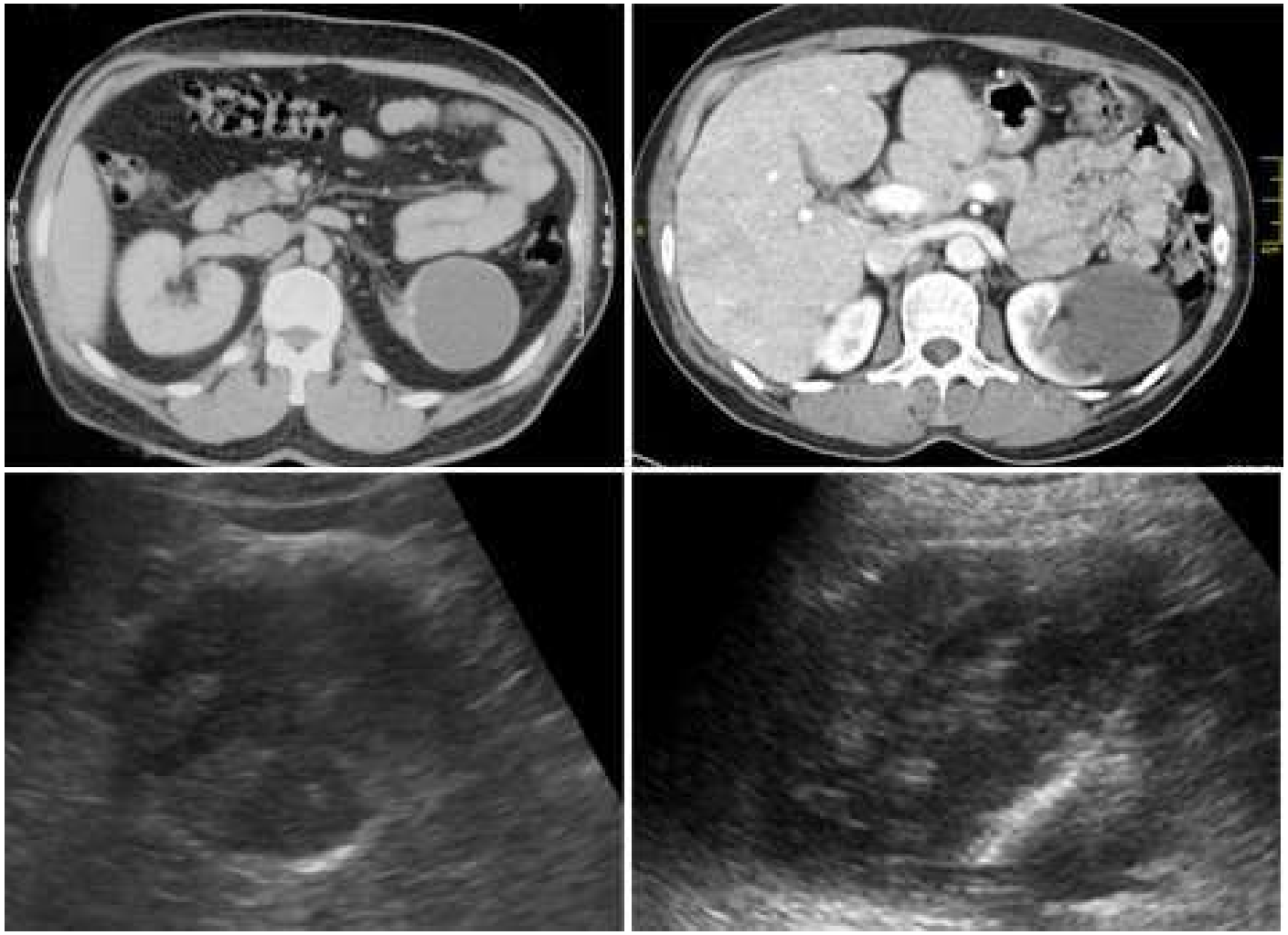


CE 2

Biliary cystadenoma

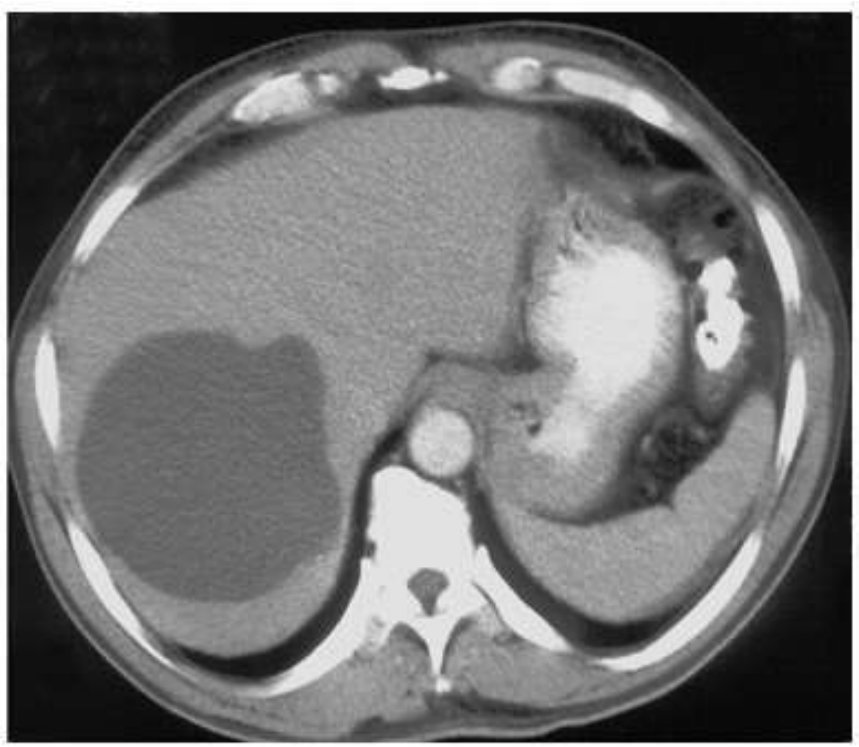
Heidelberg University Hospital



CE

Reanal cell carcinoma

Heidelberg University Hospital



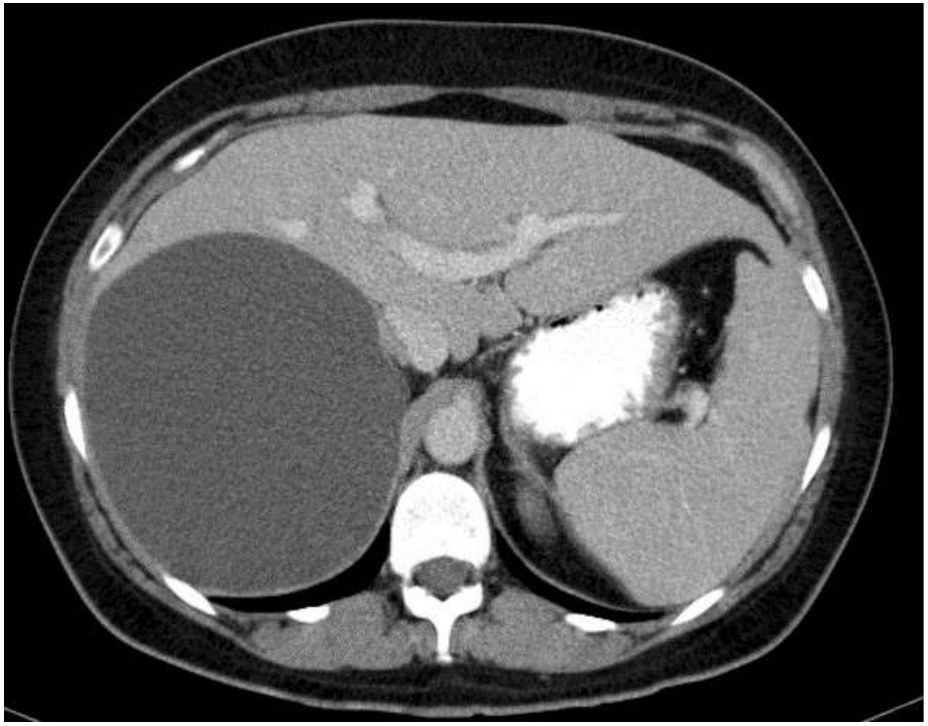
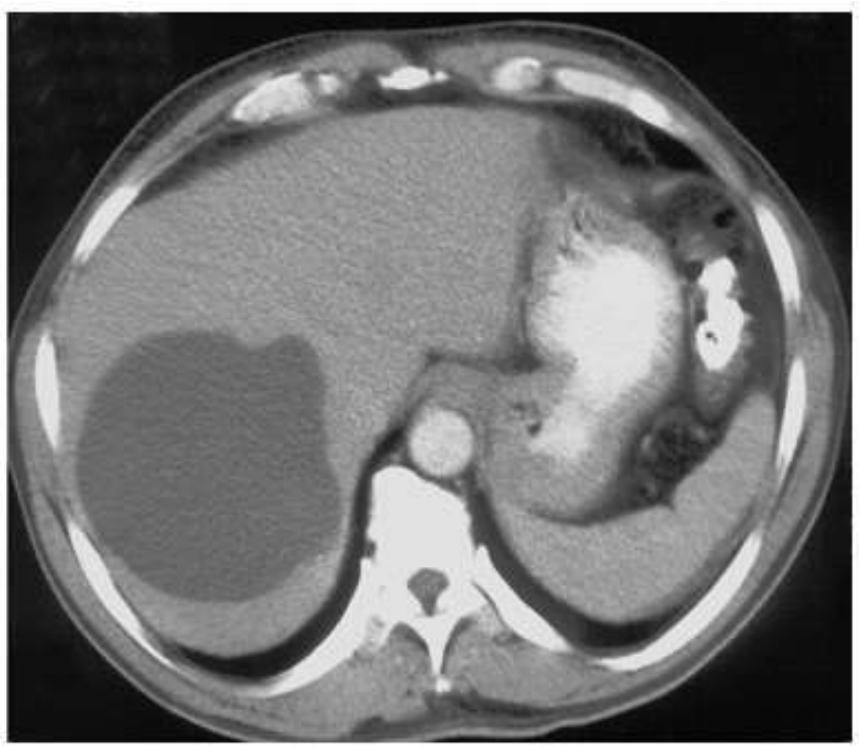
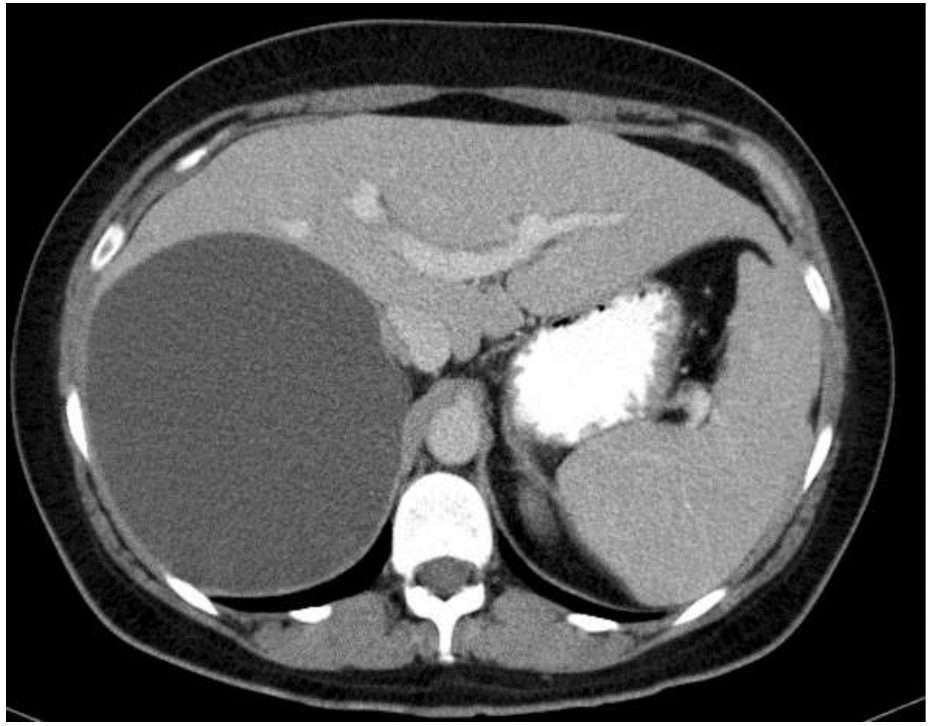


Image: Heidelberg University Hospital



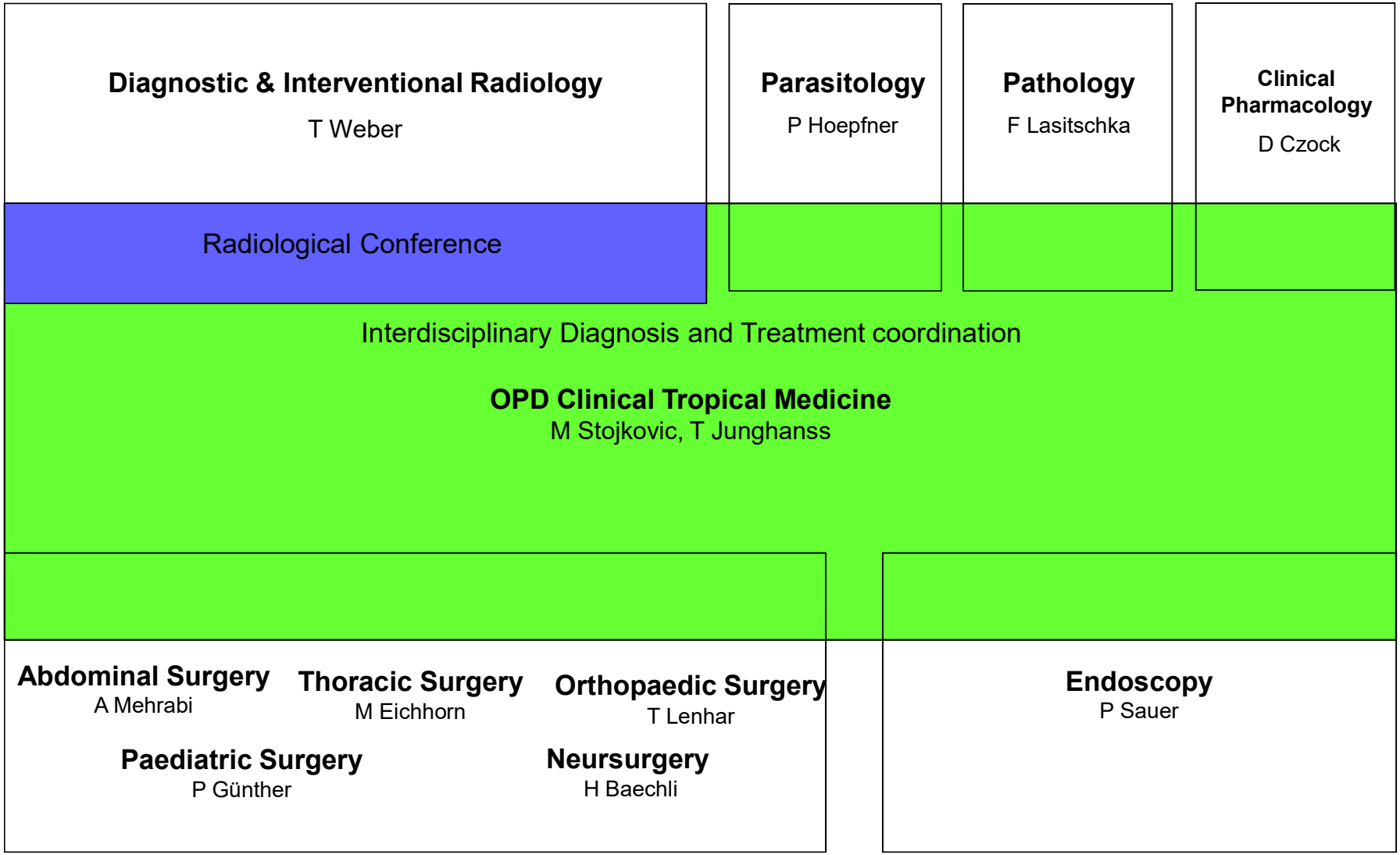
Simple cyst



CE

Image: Heidelberg University Hospital

Centre-based management of patients with Echinococcosis
University Hospital Heidelberg



Imperial Palace Mosaic Museum (image public domain)

1

WHO-IWGE IMAGING SUBGROUP: STATE OF WORK

Francesca Tamarozzi

DVM MD MSc PhD Spec Microbiologia e Virologia
WHO Collaborating Centre for the Epidemiology, Detection and Control of Cystic and Alveolar Echinococcosis, Istituto Superiore di Sanità, Roma

28° World Congress on Echinococcosis – Lima, Peru, 29-31 October 2019

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Co-coordinators: O Akhan (Turkey), F Tamarozzi (Italy)

Members
E Brunetti (Italy)
A D Karaosmanoglu (Turkey)
S Sodov (Mongolia)
L J Uchiumi (Argentina)
T Weber (Germany)

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- OBJECTIVES
- METHODS
- RESULTS
- POINTS THAT NEED CONSENSUS FROM OTHER GROUPS *
- KEY LITERATURE
- INPUT FOR RESEARCH GAP

4

OBJECTIVES

- DEFINITION OF CE CASE
- DEFINITION OF CYST STAGES BY ULTRASOUND
- OTHER IMAGING MODALITIES
- DIFFERENTIAL DIAGNOSES

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METHODS

- EXPERT CONSENSUS – DELPHI METHOD
- KEY LITERATURE contributed by members and updated by PubMed search with Boolean operators
- 3 ROUNDS OF DEBATE
  - starting from previous IWGE Expert Consensus document
  - focus on case definition and US stage definitions
  - level of agreement on proposed options

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RESULTS

TECHNICAL MANUAL DRAFT including

- Chapter/sections on Imaging diagnosis and staging
- ANNEX 1: key reference literature
- ANNEX 2: expert discussion and outcome

  Controversial issue → Expert opinions → Consensus → Research needed
- Supporting iconography on cyst stages and differential diagnoses

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MAIN DISCUSSION POINTS

ELEMENTS TO BE INCLUDED IN THE CASE DEFINITION

- **7/7 experts AGREED UPON:**

  - The diagnosis of CE is based on IMAGING

  - Serology and epidemiology may provide support to the diagnosis but cannot be used alone to define a CE case

  - Epidemiological factors* alone cannot be used to confirm a CE case when the lesion has no pathognomonic signs

  - * birth/residence/travel in endemic areas; having a personal history of CE

  - 1 experts suggested inclusion of "having relatives with CE" but it was discarded due to dependence upon the relatives living the same area as the suspect case

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MAIN DISCUSSION POINTS

IMAGING TECHNIQUES FOR CASE DEFINITION

- **HEPATIC LOCALIZATION:** 7/7 experts agreed that US alone can achieve the definition of CE confirmed case

  - MRI (T2-w and fat saturated T1-w) preferred over CT

  - CT has poor performances and should be used for post-diagnosis steps or when differential diagnosis can be based on presence of contrast enhancement

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MAIN DISCUSSION POINTS

IMAGING TECHNIQUES FOR CASE DEFINITION

- **EXTRA-HEPATIC LOCALIZATION**:

  - 3/7 experts supported the use of US alone for confirmed CE diagnosis if pathognomonic signs are clearly visible

  - 3/7 experts supported the definition of SUSPECT any lesion in extra-hepatic localization and therefore the compulsory need of other tests

  - 1/7 experts would condition the definition of confirmed CE to an extra-hepatic lesion only if hepatic CE was concomitantly present

- CONSENSUS: pathognomonic signs may be used for confirmed CE case definition but with a cautionary note on localizations where other cystic masses are more frequent (e.g. kidney, ovary, pancreas)

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MAIN DISCUSSION POINTS

INCLUSION OF SEROLOGY IN THE CASE DEFINITION *lab group

- **5/7 experts agreed** with **pragmatic approach** that takes into account that variable experience exists in recognizing confidently the pathognomonic signs of CE and that these are not always present
- 2/7 expressed concerns about the inclusion of serology in the case definition

- FINAL CONSENSUS FOR PRIMARY DIAGNOSIS → CE CASE DEFINED AS
  - presence of pathognomonic signs OR
  - no/unclear pathognomonic signs but pos in 2 screening serology (based on different antiges) OR at least 1 WB with specific band patterns OR
  - microscopy, PCR, ex-juvantibus ABZ
  - EXCLUSION if vascularization or after microscopy/PCR exclusion
  - SUSPECT no/unclear pathognomonic signs; neg serology (or only 1 non-WB +)
- CAVEATS: new cyst in previous diagnosis, extra-hepatic; CE-AE co-endemic; stages

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MAIN DISCUSSION POINTS

DEFINITIONS OF RECURRENCE AND REACTIVATION (note: no "relapse")

- **OPTION 1:** from oncology, recurrence="coming back" from any previous treatment
- **OPTION 2:** apply "reactivation" to any CE4→ CE3b and "recurrence" to residual cavity
- CONSENSUS: 7/7 TO THE USE OF OPTION 1 as option 2 would leave an ambiguity when dealing with post-percutanous lesions

* Throughout the document

RECURRENCE: appearance of an active CE stage in the **same location** where a treated cyst was located, independently of the type of previous treatment

REACTIVATION: in **spontaneously inactivated CE4** cysts, appearance of daughter vesicles in the solid matrix, i.e. evolving in a CE3b stage.

NEW CE CYST: appearance of a new CE cyst in a place different from where a CE cyst was diagnosed before.

SECONDARY ECHINOCOCCOSIS: appearance of one or more echinococcal cysts in serosal cavities due to spillage of cyst content

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MAIN DISCUSSION POINTS

APPROPRIATENESS OF CURRENT WHO-IWGE CLASSIFICATION

- 6/7 experts agreed that the WHO-IWGE classification would require come changes to avoid confusion especially arising from CE3 → CE3a and CE3b
- CONSENSUS:
  - keep using the same classification to avoid too frequent changes
  - MAKE DESCRIPTIONS AND DEFINITIONS MORE CLEAR AND STRINGENT
  - privilege the staging and viability concepts over "activity" to guide approach
  - clear indication the "activity" refers just to the evolutionary condition of the cyst

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MAIN DISCUSSION POINTS

FEATURES DEFINED AS "PATHOGNOMONIC"

- 5/7 experts agreed on the use of "pathognomonic" to define diagnostic features
- 1/7 experts would prefer "diagnostic feature"
- 1/7 experts had no preference

- CONSENSUS: pathognomonic features, with special reference to the hepatic localization, are described in detailed, including interpretation of (lack of) vascularization

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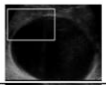
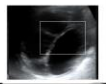
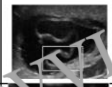
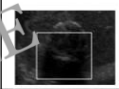
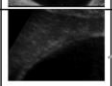
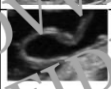
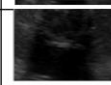
MAIN DISCUSSION POINTS

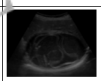
CL: to leave it or not to leave it in the document?

- 5/7 experts would have preferred to ELIMINATE CL from the pictorial description of CE
- 1/7 expert suggested to consider CL as CE until proven otherwise in endemic areas
- 6/7 experts agreed that the visualization of a single wall can be a feature also of biliary cysts and therefore this feature is not enough to characterize a CE1 stage

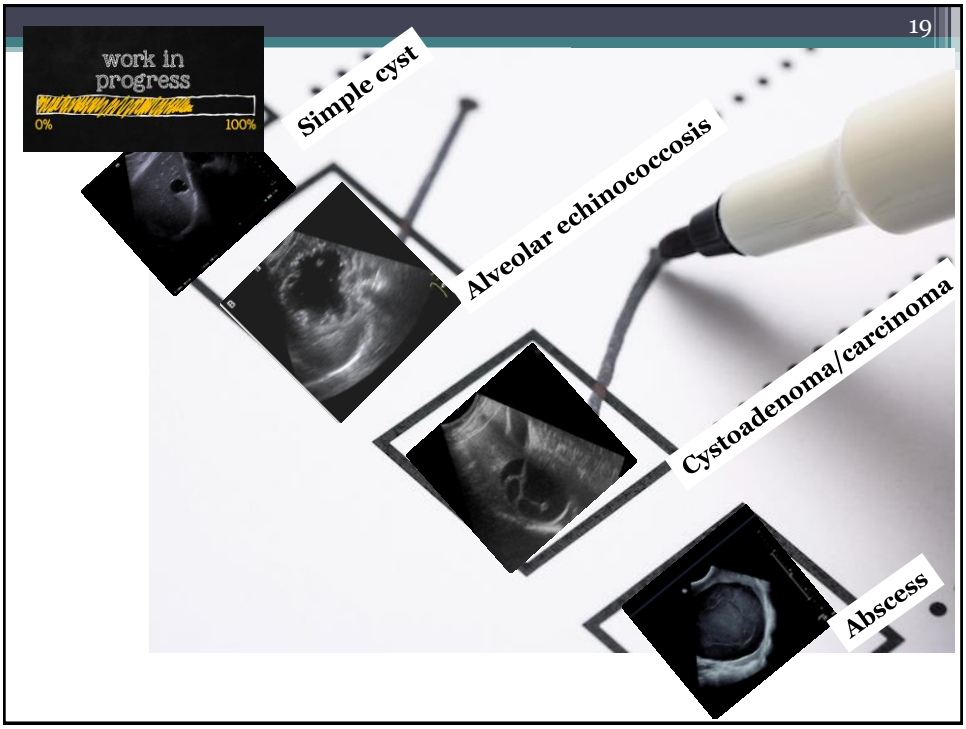
- CONSENSUS:
  - maintain CL in the document (on the basis of avoiding too many changes)
  - make more clear that CL = SUSPECT and it is not a CE stage (even in endemic areas)
  - indicate only the double wall sign as pathognomonic of CE1

1) **Imaging-based case definition is operator-dependent**,
2) **Information on immunodiagnostic tests results and on epidemiological setting only provides circumstantial supporting evidence** favouring the diagnosis of CE but cannot be used alone to define a CE case
3) **Extra-hepatic lesions should be considered suspect until proven otherwise when clear-cut pathognomonic signs are not clearly visible**, particularly in organs that are rare locations for CE but common locations for other cystic lesions (e.g. kidney, ovary, pancreas).
4) **Serology tests have low sensitivity for CE1, CE4 and CE5 stages and for CE cysts in any stage in extra-hepatic localization.**
5) **Serology tests highly cross-react with alveolar echinococcosis**, therefore specific tests for AE are imperative in CE-AE co-endemic areas to differentiate CE from AE if imaging does not allow differentiation

	ECHINOCOCCAL CYSTS						SUSPECT
US image							
Particular of the pathognomonic sign							
STAGE	CE1	CE2	CE3	CE3b	CE4	CE5	CL
VIABILITY	Viable	Viable	Viable or non-viable	Viable	Low viability or non-viable	Non-viable	

Stage	Short description	Detailed description	Pathognomonic features	Macroscopic appearance	Example US image	Viability	Activity grouping
CE1	Univesicular, liquid content	Well defined univesicular cyst, with round or oval shape, anechoic content and posterior acoustic enhancement, with or without low-intensity floating echoes upon decubitus change (moving "hydatid sand") and with visible pathognomonic "double wall sign" consisting in the inner hyperechoic laminated layer and outer hypoechoic adventitial layer.	**Double wall sign** consisting in the inner hyperechoic laminated layer and the outer hypoechoic adventitial layer	External surface of the wall: pearl-white. Content: clear fluid (possibly bile-stained if connection with the biliary tree); possibly floating "hydatid sand" composed of brood capsules and protoscolices. Inner surface of the wall: whitish-appearance, with velvety texture		Viable	Active
CE2	Multivesicular, liquid content	Well defined multivesicular cyst, with round or oval shape, posterior acoustic enhancement, one or more daughter vesicles filling in part or completely the cyst; the pathognomonic "honeycomb" appearance is provided by the thin, regular, continuous and avascular, clearly distinguishable adjacent walls of juxtaposed daughter vesicles	**Honeycomb** appearance provided by the thin, regular, continuous and avascular, clearly distinguishable adjacent walls of juxtaposed daughter vesicles	External surface of the wall: see CE1 Content: clear fluid (possibly bile-stained if connection with the biliary tree); fluid-filled daughter vesicles, of different sizes.		Viable	Active
CE3a	Univesicular, liquid content with detached laminated layer	Well defined univesicular cyst, with round or oval shape, posterior acoustic enhancement, and with partial or complete detachment of the laminated layer, visible as a hyperechoic thin and regular membrane floating in the anechoic cyst content, giving the pathognomonic appearance, referred to as the "water lily sign". The whole membrane must be identified as continuous hyperechogenic structure, in different incidences. Low-intensity floating echoes upon decubitus change (moving "hydatid sand") may be present.	**Detached laminated layer (referred to as "water lily sign")** consisting in the continuous hyperechoic thin and regular membrane floating in the anechoic cyst content	External surface of the wall: see CE1 Content: clear or bile-stained fluid (possibly bile-stained in connection with the biliary tree); the detached laminated layer has a gelatinous aspect.		Viable or not viable	Transitional
CE3b	Multivesicular, solid content with daughter vesicles	Well defined multivesicular cyst with round or oval shape, posterior acoustic enhancement and heterogeneous structure, encompassing avascular solid components and hypoechoic folded structures, deriving from degenerating membranes, and one or more liquid daughter vesicles with anechoic content, giving, together, the pathognomonic "swiss cheese" appearance.	**Swiss cheese appearance** provided by the presence of fluid-filled daughter vesicles in a heterogeneous solid content showing the hypoechoic folded membranes	External surface of the wall: see CE1 Content: solid/semi-solid (resembling mashed peas) containing whitish membranes and one or more fluid-filled daughter vesicles of different sizes.		Viable	Transitional
CE4	Solid content	Well defined round or oval mass with or without posterior acoustic enhancement and with heterogeneous avascular solid content formed by the degenerated cyst membranes, and hypoechoic folded structures deriving from degenerating membranes in the mass and giving the pathognomonic "ball of wool" or "canalicular" or "cerebroid" appearance.	**Ball of wool or canalicular or cerebroid appearance** resulting from the hypoechoic folded cyst membranes visible in the echogenic cyst content	External surface of the wall: see CE1 Content: solid/semi-solid (resembling mashed peas) containing whitish degenerated membranes		Low viability or not viable	Inactive
CE5	Solid content with eggshell calcified wall.	Well defined round or oval mass with posterior acoustic shadow deriving from a complete or nearly complete egg-shell calcified wall, and heterogeneous avascular solid content (when acoustic shadow allows visualization) formed by the degenerated cyst membranes and hypoechoic folded structures deriving from degenerating membranes in the mass and giving the pathognomonic "ball of wool" or" canalicular" appearance.	When acoustic shadow allows visualization: **ball of wool or canalicular appearance** resulting from the hypoechoic folded cyst membranes visible in the echogenic cyst content	External surface of the wall: partly or completely calcified Content: solid/semi-solid (resembling mashed peas) containing whitish degenerated membranes		Not viable	Inactive

ABDOMINAL ORGANS		
Stage	**MRI**	**CT**
CE1	A CE1 cyst may not be confidently differentiated from simple liver cysts on MRI images. A CE1 cyst is univesicular, well defined, homogenously hyperintense, on heavily T2-weighted images. The cyst content is isointense to CSF on T2-weighted images. The cyst is homogeneously hypointense in pre-contrast T1-weighted sequences. A cyst wall may be discernible but its presence is not pathognomonic for CE. On post-contrast T1-weighted images, there may be slight enhancement of the cyst wall.	A CE1 cyst may not be confidently differentiated from simple liver cysts on CT images. A CE1 cyst appears as a well-defined lesion that is homogeneously hypodense with a HU value ranging between 0-20. A cyst wall may be discernible, however this finding is not pathognomonic for CE. On post-contrast images, slight enhancement of the cyst wall may be seen. Wall calcifications may be rarely detected.
CE2	Well-defined multivesicular cyst partially or completely filled with one or more daughter vesicles. These vesicles are best visualized on heavily T2-weighted images. On post-contrast T1-weighted images, there is no enhancement of cyst contents. On post contrast T1-weighted images there may be slight enhancement of the cyst wall.	The multivesicular content of CE2 cysts is not reliably discerned with CT. The walls of the daughter vesicles may be slightly hyperdense compared to the fluid content of the cyst. On post-contrast images, there is no enhancement of cyst contents. There may be slight enhancement of the cyst wall after contrast injection. Wall calcifications may be occasionally present.
CE3a	Well-defined univesicular cyst with detached laminated layer that is best visualized on heavily T2-weighted images. The detached layer is hypointense compared to the cyst fluid on T2-weighted images. The normal detached layer occasionally appears hyperintense compared to the cyst fluid on T1-weighted images. The cyst fluid is isointense to CSF on heavily T2-weighted images. On post-contrast T1-weighted images there is no enhancement of cyst contents whereas slight enhancement of the cyst wall may be detected.	The detached laminated layer may not be reliably detected on CT images. This layer can be slightly hyperdense compared to the fluid content of the cyst. On post-contrast images, typically there is no enhancement of the cyst contents. Slight contrast enhancement of the cyst wall may be. Wall calcifications may occasionally be present.
CE3b	Well-defined cyst partially filled with one or more daughter vesicles that are visualized best on heavily T2-weighted images. The cyst content between daughter vesicles generally appears solid and of variable signal intensity on T2-weighted images. The cyst content between daughter vesicles may be moderately hyperintense on T2-weighted images compared to liver parenchyma but hypointense to CSF. Cyst content may appear iso- or hypointense compared to the liver parenchyma on T2-weighted images. There is no enhancement of the cyst contents on post-contrast T1-weighted images whereas slight enhancement of the cyst wall may be observed.	The presence of daughter vesicles in CE3b cysts may not be evident on CT images. The solid parts of the cyst content generally have HU values greater than 20. Within the cyst matrix, daughter vesicles may be visible. On post-contrast images cyst content does not enhance. Slight contrast enhancement of the cyst wall may be seen. Wall calcifications may be present.
CE4	Completely solid-looking lesions having variable signal intensity on T2-weighted images. Signal intensity on T2-weighted images may range from moderately hypointense to significantly hypointense compared to the liver parenchyma. The T2 signal is lower than CSF on heavily T2-weighted images. The cyst content may be moderately heterogeneous with a "canalicular" appearance. Degenerating cyst membranes may be hypointense or hyperintense compared to the other cyst content on heavily T2-weighted images. Enhancement is not present after contrast injection on T1-weighted images.	The HU values of the CE4 cysts vary, but are usually greater than 20 HU. The cyst content may be moderately heterogeneous with a "canalicular" appearance. Degenerating cyst membranes are usually hypodense compared to the other cyst content. On post-contrast images, typically there is no enhancement within the cyst. Wall calcifications are frequently present.
CE5	As calcifications may not be reliably detected with MRI, this modality may be of limited use for characterizing CE5 cysts. However, MRI may be of help in characterizing cysts difficult to define on ultrasound due to marked calcification. Most lesions considered CE5 on ultrasound are not hyperintense in T2-weighted sequences compared to the liver parenchyma. In post-contrast T1-weighted images there is no enhancement.	Dense mural calcifications are the typical imaging finding of CE5 cysts. Internal calcification may be observed in adjunct to mural calcifications. The cyst content may be moderately heterogeneous with a "canalicular" texture. On post-contrast images, enhancement of the cyst wall or the cyst content is typically not detected.



KEY LITERATURE

INCLUSION

- original research including cohort studies, case-control studies, and cross-sectional studies
- clear description of CE and non-CE case definition
- cyst staging based on ultrasound reported (where relevant for the question)
- follow-up length and loss to follow-up rate reported (where relevant for the question)
- extractable question-relevant data

EXCLUSION

- reviews, case reports, letters to the editor and opinion papers not presenting original data
- absence of data on cyst staging and follow-up details, where relevant for the question

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KEY LITERATURE

QUESTION	REFERENCES
How do CT and MRI perform compared to US in depicting features diagnostic for CE stages?	Diagnosis and staging of cystic echinococcosis: how do CT and MRI perform in comparison to ultrasound? PLoS Negl Trop Dis 2012
	Differentiation between hepatic cystic echinococcosis types 1 and simple hepatic cysts: A retrospective analysis Medicine (Baltimore) 2019
	The role of diffusion- weighted magnetic resonance imaging in the classification of hepatic hydatid cysts. Eur J Radiol 2013
	Is it possible to differentiate between hydatid and simple cysts in the liver by means of diffusion-weighted magnetic resonance imaging? Clin Imaging 2012
	The role of diffusion-weighted MRI in the classification of liver hydatid cysts and differentiation of simple cysts and abscesses from hydatid cysts Diagn Interv Radiol 2010
	Diffusion-Weighted Imaging in the Differential Diagnosis of Simple and Hydatid Cysts of the Liver. Am J Roentgenol 2007
What is the inter and intra-assessor agreement in CE cyst staging using the WHO-IWGE classification?	Expert Reliability for the World Health Organization Standardized Ultrasound Classification of Cystic Echinococcosis. Am J trop med Hyg 2017
Is there a correspondence between CE cyst stages and cyst viability, with special regards to transitional and inactive stages?	Metabolic viability assessment of cystic echinococcosis using high-field 1H MRS of cyst contents. NMR Biomed 2008
	The role of calcification for staging cystic echinococcosis (CE). Eur Radiol 2007
	Long-term sonographic and serological follow-up of inactive echinococcal cysts of the liver: hints for a watch-and-wait approach. PLoS Negl Trop Dis 2014
	Watch and wait approach for inactive echinococcal cysts of the liver: an up-date. Am J Trop Med Hyg 2018
	Medical treatment versus "watch and wait" in the clinical management of CE3b echinococcal cysts of the liver. BMC Infectious Diseases 2014
	Watch and wait management of inactive cystic echinococcosis – does the path to inactivity matter – analysis of a prospective patients cohort. PLoS Negl Trop Dis 2016
(i) What is the proportion of cysts classified as CL the nature of which is parasitic (i.e. CE1)?; (ii) can the sole visualization of a single cyst wall on conventional US abdominal imaging reliably indicate the echinococcal nature of a CL lesion?	The natural history of cystic echinococcosis in untreated and albendazole-treated patients. Acta Trop 2017
	Prevalence of abdominal cystic echinococcosis in rural Bulgaria, Romania, and Turkey: a cross-sectional ultrasound-based population study from the HERACLES project. Lancet Infect Dis 2018.
	Sonographic diagnosis of hydatidosis: the sign of the cyst wall. Eur J Ultrasound 2003.

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RESEARCH GAPS

TOPIC	RESEARCH GAPS
INCLUSION OF SEROLOGY IN CE CASE DEFINITION	Standardization and thorough testing of standardized serology assays for CE
	Role of serology in the CE diagnosis algorithm; usefulness of (standardized) serology for clinical decision-making stratified by pre-test probability and cyst stage
SUGGESTIVE EPIDEMIOLOGICAL FACTOS	Impact of epidemiological history on clinical decision-making
	Clear epidemiological risk factors still poorly defined
APPROPRIATENESS OF THE WHO-IWGE CLASSIFICATION	Further testing of the inter- and intra- observer reliability of the classification on personnel with different expertise levels
	Research on markers of biological viability of cysts independently of the activity status on ultrasound
PATHOGNOMINC IMAGING FEATURES	Proportion of “CE” diagnosis based on visualization of “pathognomonic” imaging features alone, confirmed as CE with other modalities (possibly stratified by experience of the sonographer)
HOW TO CONSIDER CL	Proportion of CL being CE or not (stratified by organ localization and endemic/non-endemic area)
CE CASE IN EXTRA-HEPATIC LOCALIZATION BASED ON IMAGING ALONE	Proportion of lesions diagnosed as CE with imaging alone being really CE after further investigation
RECURRENCE VS REACTIVATION	Is there any substantial difference (biological, clinical) in the reactivation of spontaneously inactivated cysts *VS* of cysts inactivated/removed after therapy?

THANKS FOR YOUR ATTENTION

QUESTIONS?