



# Ongoing SIOPEL studies PHITT protocol

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Members of the SIOPEL radiological sub-committee

PHITT European central reviewers



**ESPR**  
European Society of  
Paediatric Radiology



# Plan

- Some definitions
- Short history of SIOPEL protocols- PHITT protocol
- Imaging evaluation – PRETEXT Classification from 2005 to 2017
- Ongoing work

# Some definitions

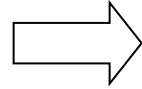
## What are SIOPEL, PHITT and PRETEXT?

- SIOPEL: liver tumour group in the European Society of paediatric oncology – first protocols on liver cancers
- PHITT: Paediatric Hepatic Tumour International Trial
- PRETEXT: Pre TreatTment EXTension based on imaging

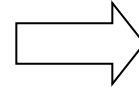
# Hepatoblastoma - European strategy- SIOPEL (from 1987 to 2017 )

## Diagnosis

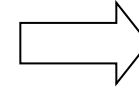
- PRETEXT  
1992 - 2005
- Biopsy



Neoadjuvant  
chemotherapy  
( 2 – 3 mths )



S  
U  
R  
G  
E  
R  
Y



+/- Adjuvant  
chemotherapy  
( 2 m )





# SIOPEL studies

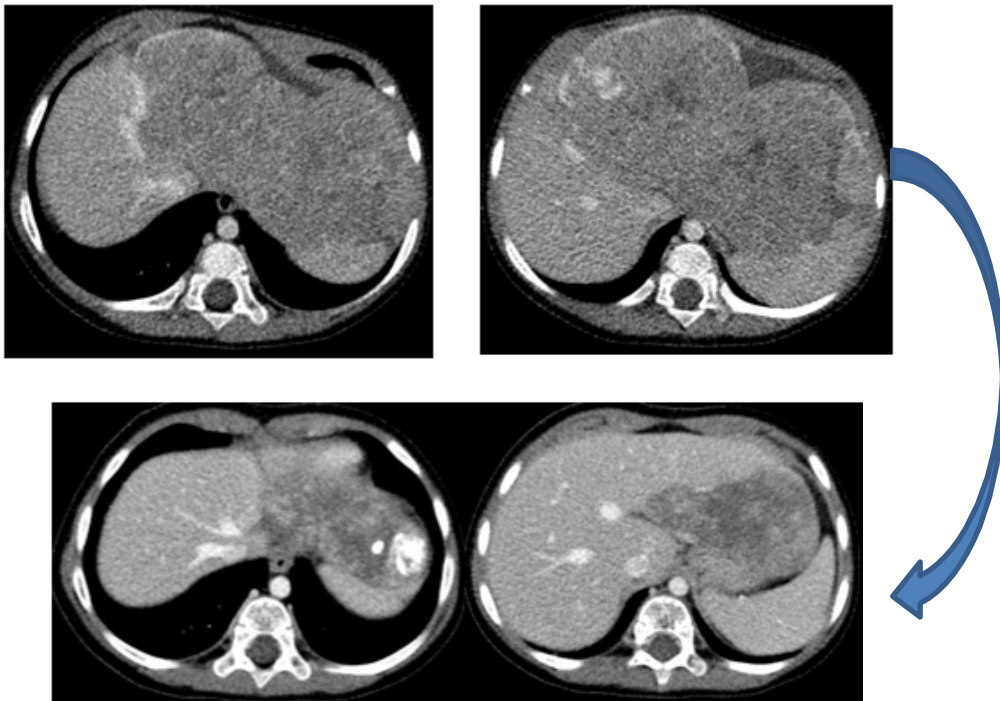
SIOPEL 1	PLADO for all HBL	1990 - 1994
SIOPEL 2	Cisplatin alone for SR (Standard Risk)HBL	1995 - 1998
SIOPEL 3	PLADO vs Cisplatin for SR HBL	1998 – 2006
SIOPEL 4	High risk HBL pilot study	2005 - 2009
SIOPEL 6	SR HBL cisplatin vs Cisplatin+STS	2007 - 2014
Phase II	Cyclophosphamide	1995 - 2001
Phase II	Irinotecan ( CPT 11 )	2003-2008

**PRETEXT 1992**

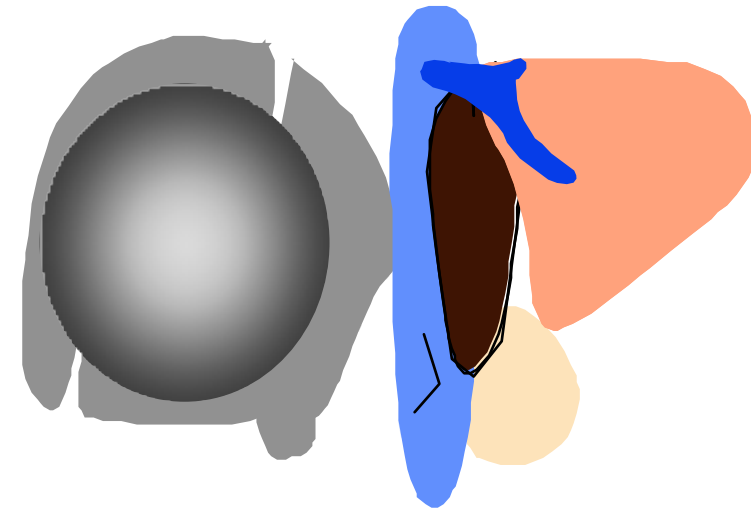
**PRETEXT 2005**

# Hepatoblastoma treatment

## Cisplatin for chemotherapy



## Complete resection is necessary



**Event-free survival from 25 % in the 70's to more than 75% !**

# In 2017, International initiative



- International trial: European + North American (COG) + Japanese
- Goal : to give the treatment “As Low As Reasonably Achievable” according to the characteristics of the tumour
- **Risk group stratification**

# Risk group stratification

PRETEXT nb + Metastasis + Annotation factors

V: hepatic vein  
P: portal vein  
E: extrahepatic extension  
F: multifocal  
R: rupture

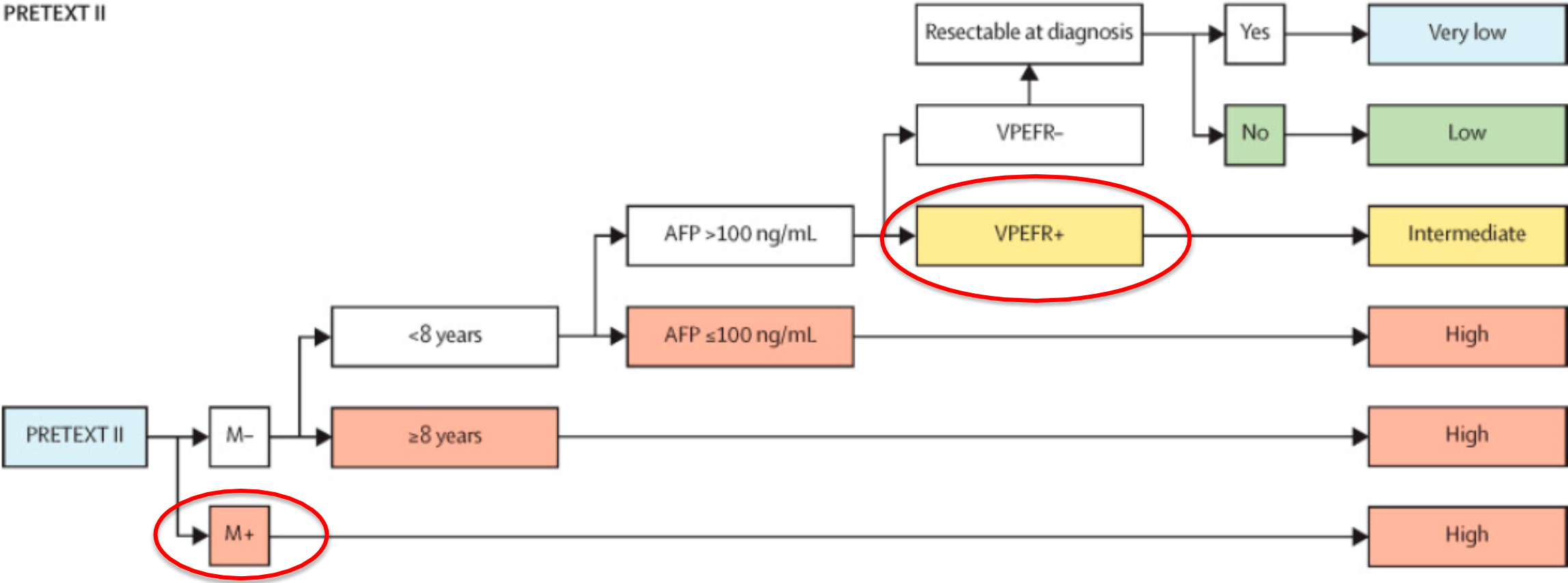
New PRETEXT Classification 2017

- Age:  
+ <3 years  
>8 years
- AFP:  
<100  
100-1000

= Risk group

A. very low  
B. Low  
C. Intermediate  
D. High

PRETEXT II





# 2017 PRETEXT: radiologic staging system for primary hepatic malignancies of childhood revised for the Paediatric Hepatic International Tumour Trial (PHITT)

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# Recommendations for imaging in PHITT (2017 PRETEXT)

- **MRI** recommended at diagnosis and for evaluation during treatment
  - Under GA
  - With hepato-specific contrast
  - = not feasible in all european countries
  - **Very good detection of lesions**
- **Abdominal CT** not necessary if MRI performed...
  - Sometimes necessary for vessels assessment

Table 1 Sample MRI protocol using a hepatocyte-specific contrast agent [21]

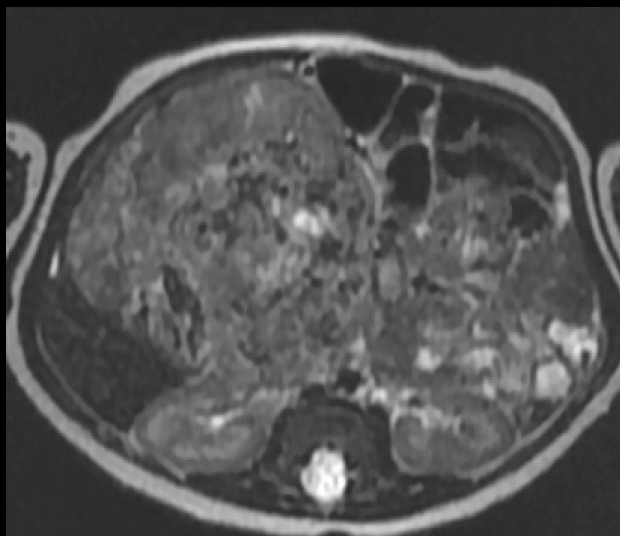
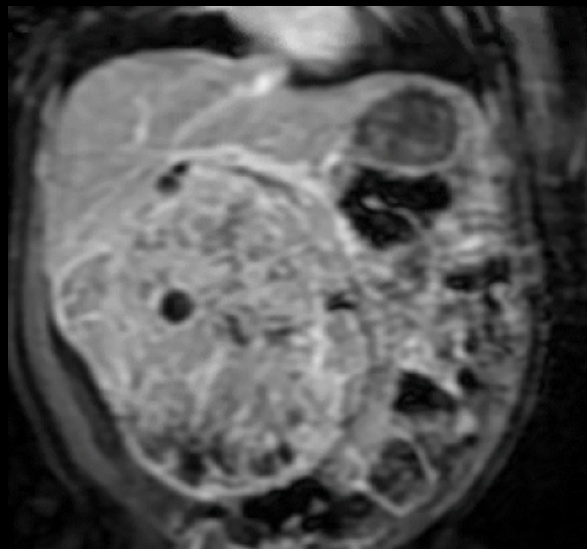
MRI sequence	Rationale
Axial T2-weighted fast-spin echo with fat suppression	Detection of fluid/edema; many tumors are hyperintense to normal liver
Axial T1-weighted fast spin echo	Detection of macroscopic fat and blood products Visible vascular flow voids help with PRETEXT staging
Axial T1-weighted in-opposed-phase	Signal loss on opposed-phase images indicates presence of fat
Axial T1 pre 3-D SPGR	Allows for comparison with post-contrast images
Axial T1-weighted post dynamic 3-D SPGR (arterial, portal venous, and late portal venous phases)	Assessment of enhancement characteristics
Axial 2-D time-of-flight	Assessment of vasculature; can be used to problem-solve if other sequences are degraded by motion
Axial diffusion-weighted imaging	Detection of highly cellular masses
Coronal 3-D T2-weighted FSE	Isotropic 3-D sequences allow for reconstruction in multiple imaging planes. Assessment of biliary tree
Axial T1-weighted 3-D SPGR hepatocyte phase	Functioning hepatocytes retain contrast —important for lesion characterization
Coronal T1-weighted 3-D SPGR hepatocyte phase	Additional imaging plane improves lesion detection/localization Assessment of central biliary tree

FSE, fast spin echo; PRETEXT, pretreatment extent of disease; SPGR, spoiled gradient recalled echo



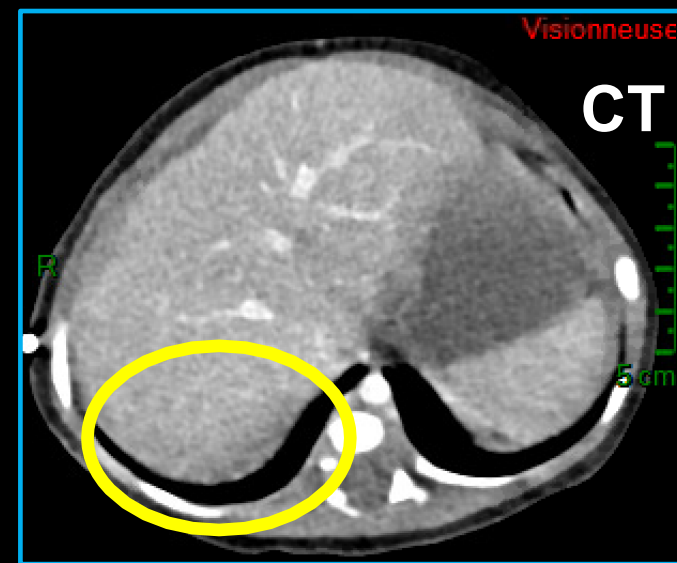
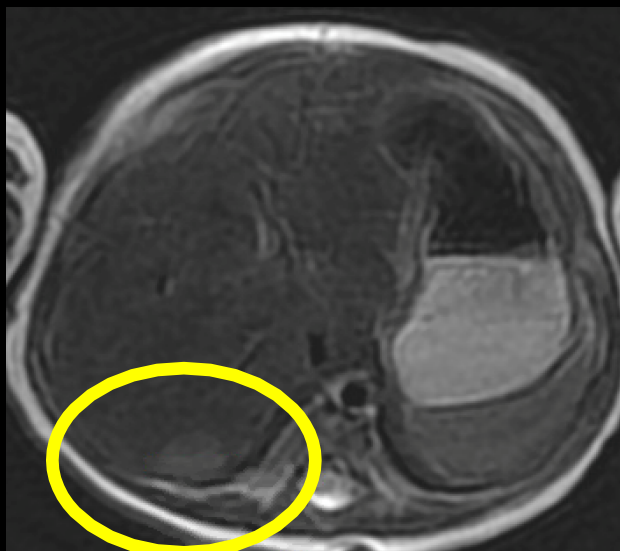
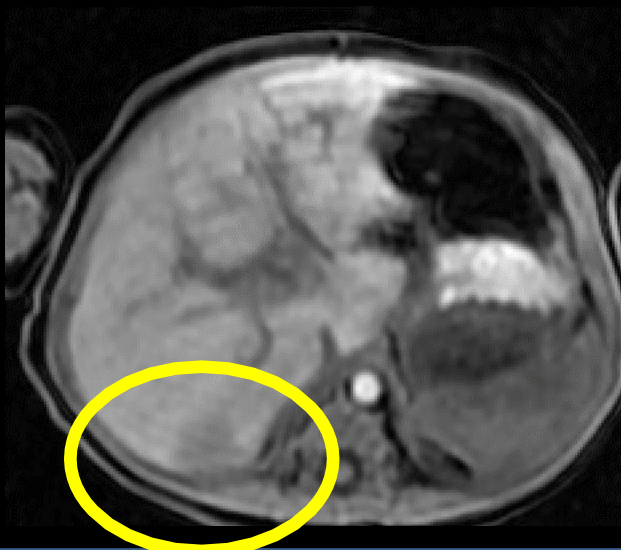
2 mo baby

AFP= 259 580  $\mu\text{g/ml}$



Large tumour + small nodule in Sgt VII

MRI >> CT

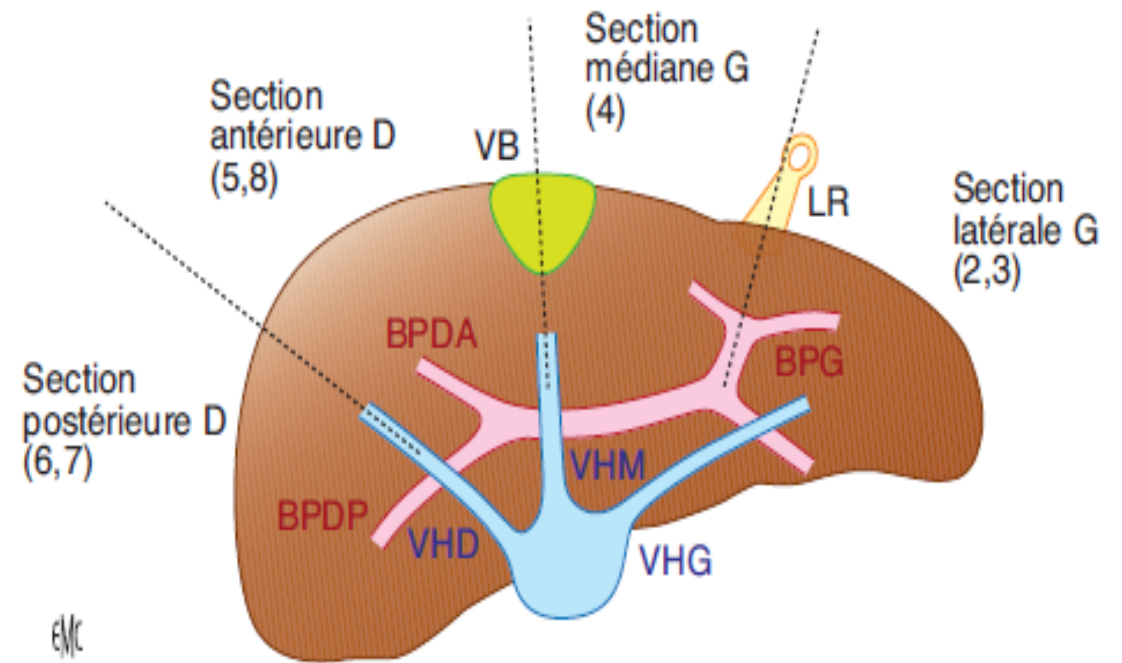
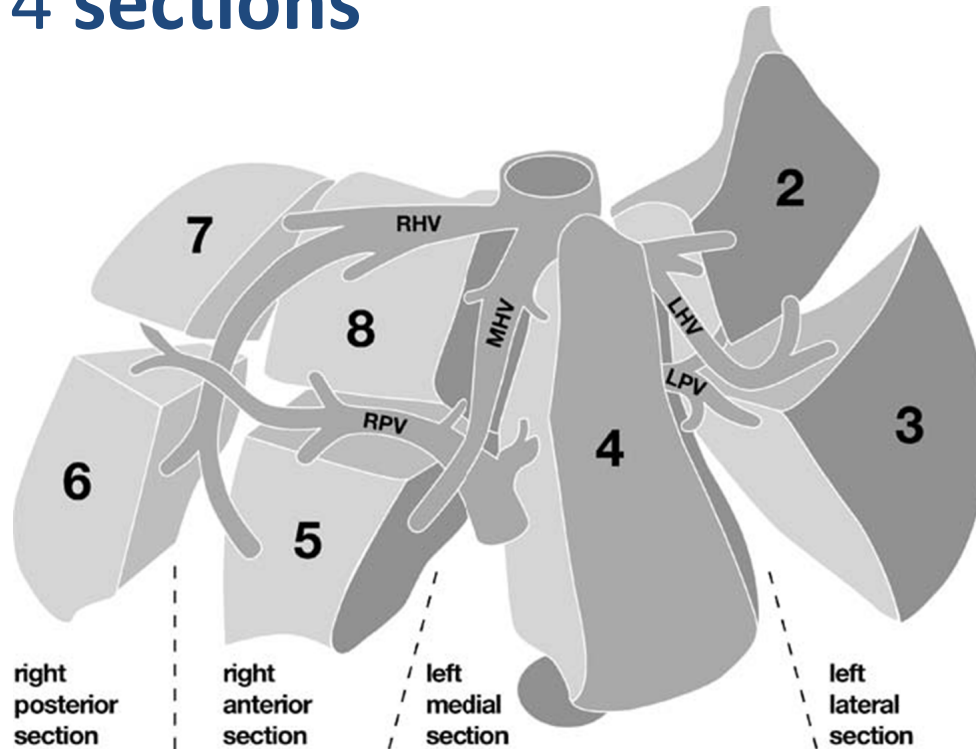




# Classification PRETEXT 2005- 2017

## PRE Treatment EXTent of tumor system

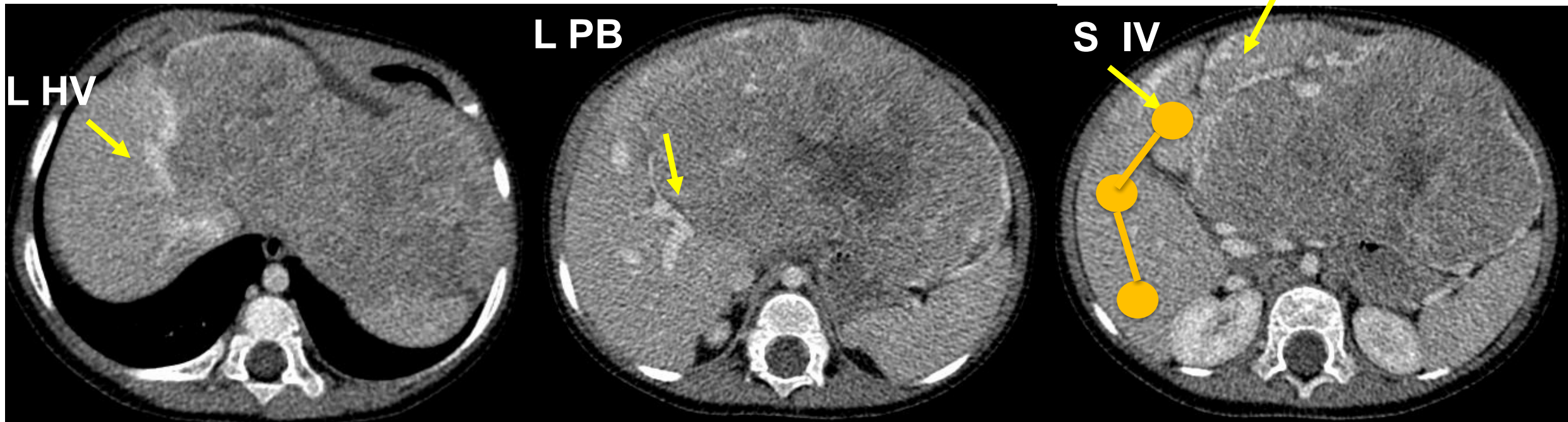
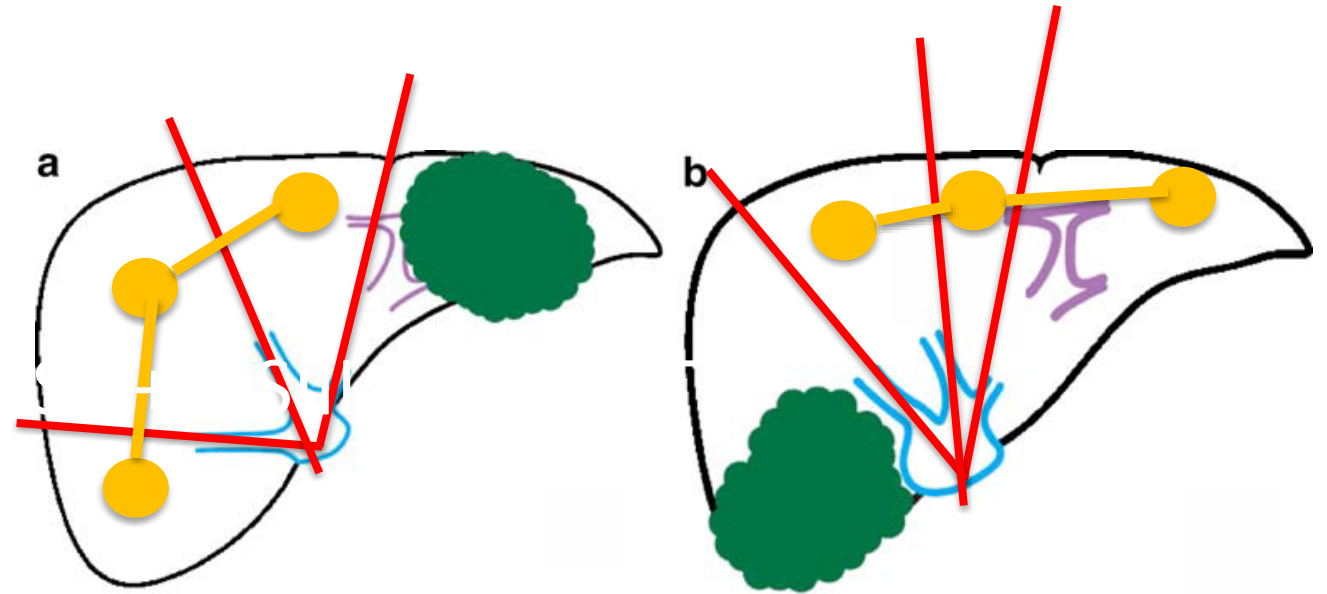
- 4 sections



PRETEXT number = 4 – number of adjoining sections free of disease

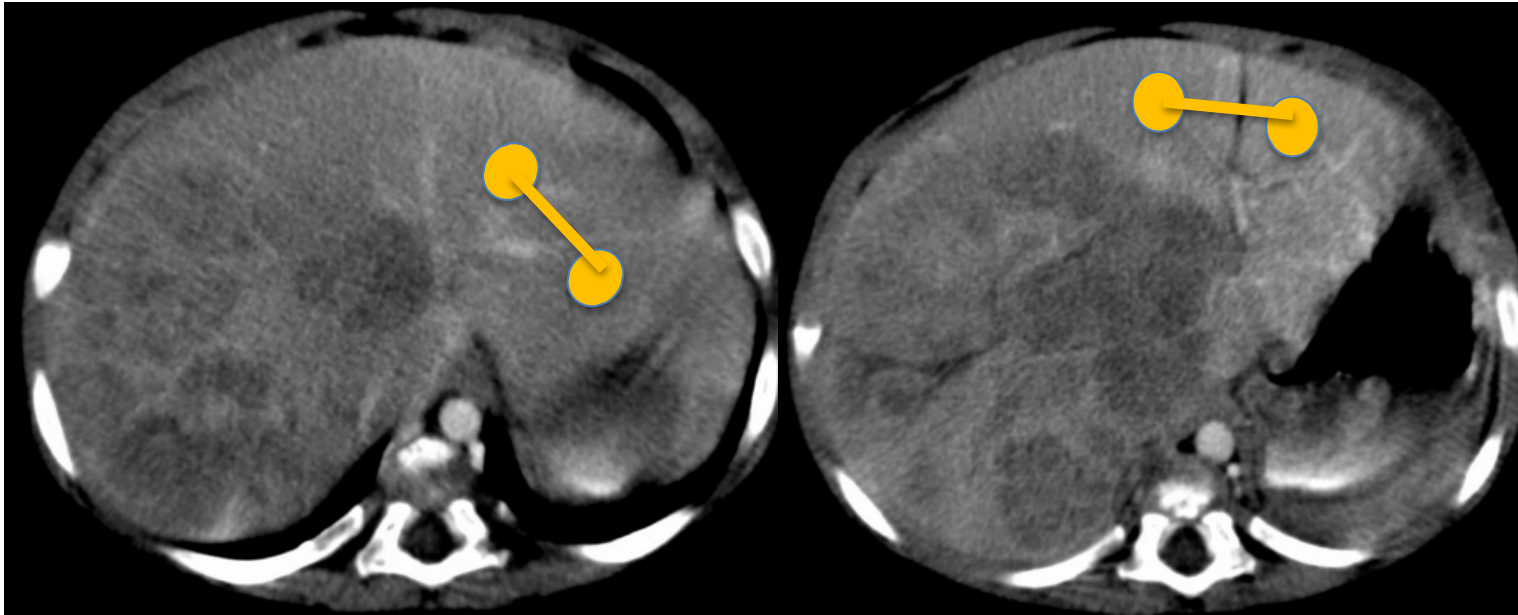
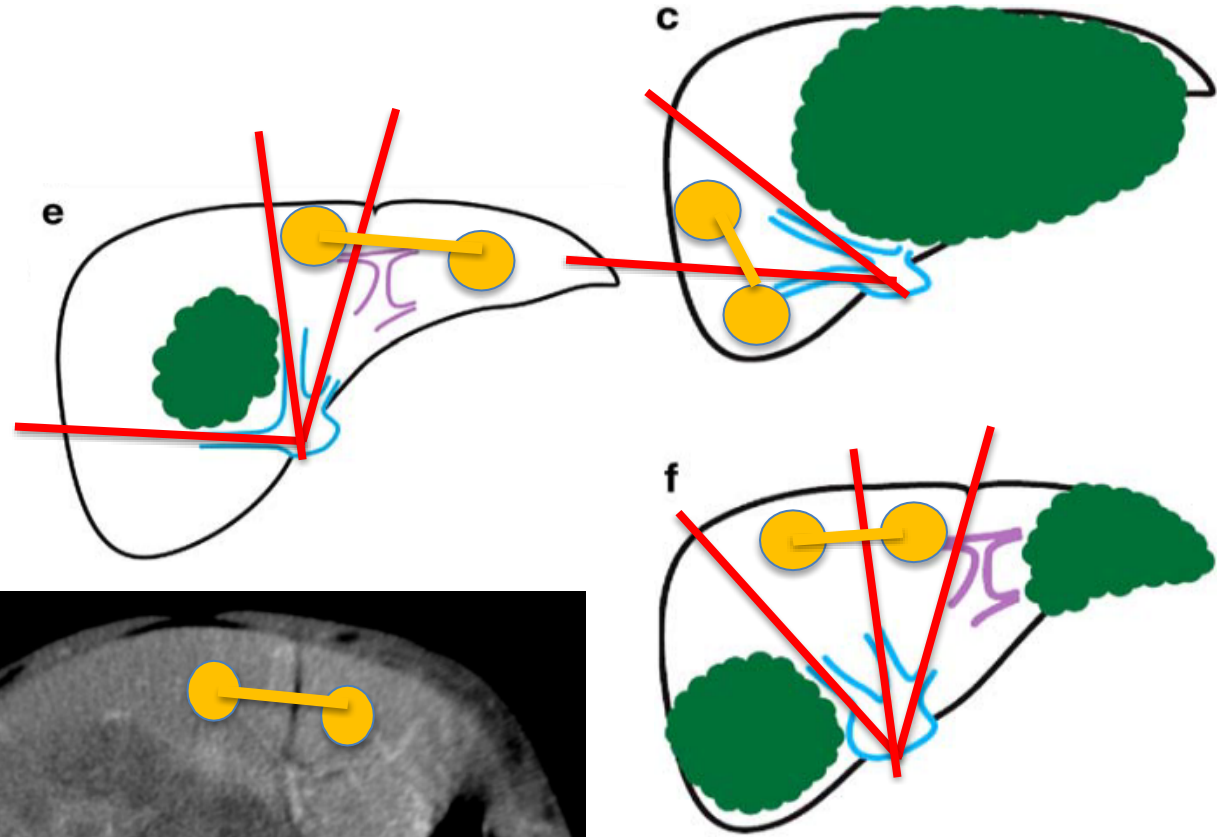
# PRETEXT I

- **PRETEXT I:**  
3 adjoining sections free



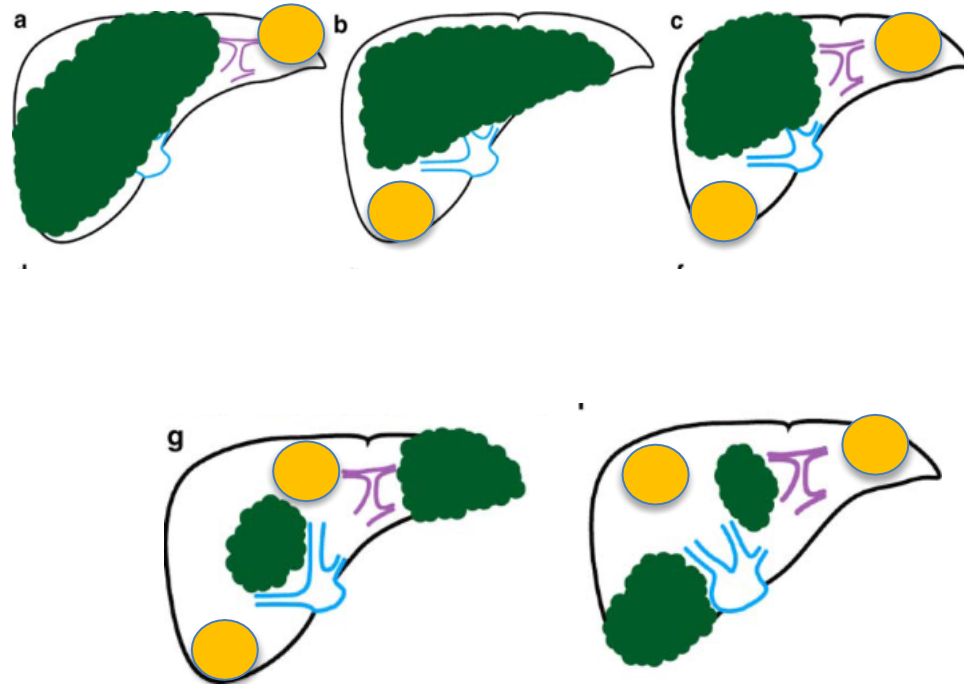
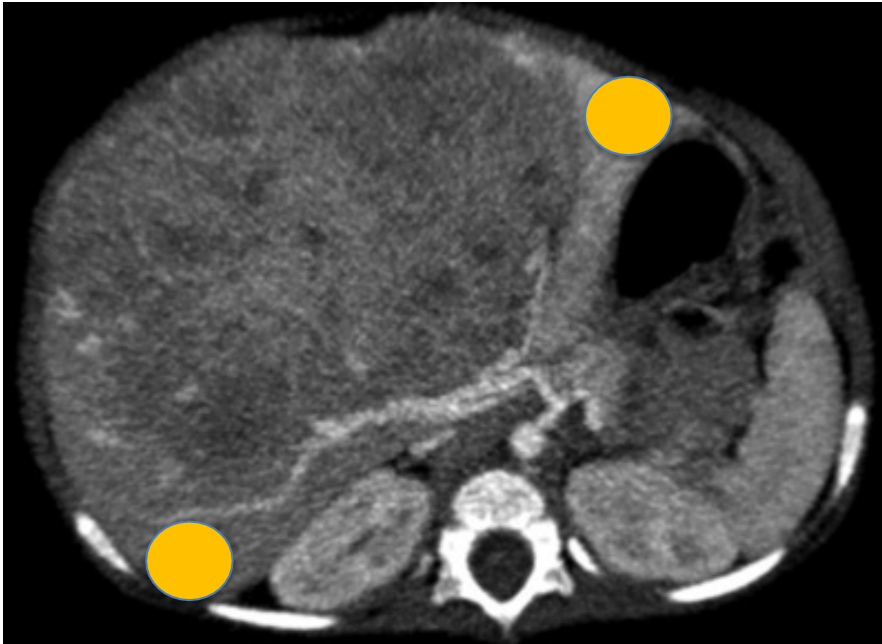
# PRETEXT II

- **PRETEXT II** : 2 adjoining sections free
- And / or caudate lobe



# PRETEXT III

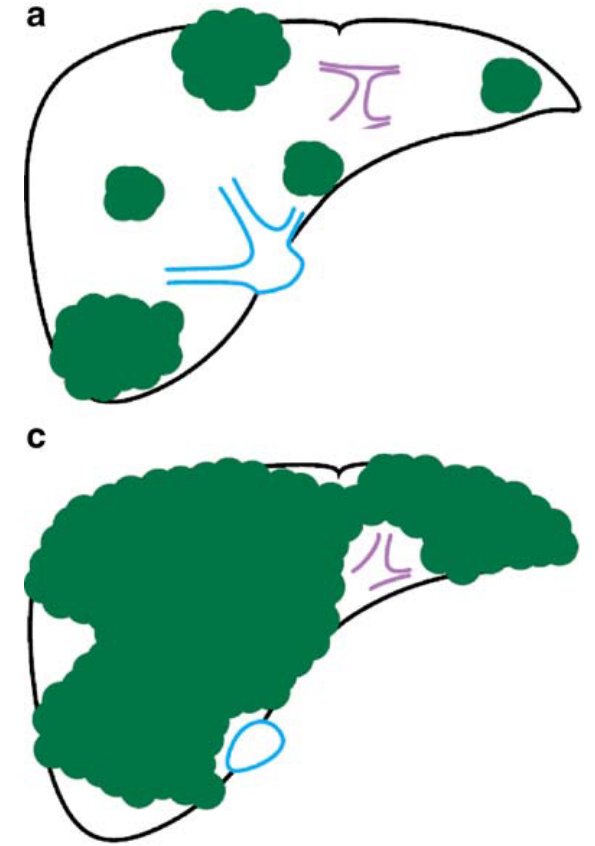
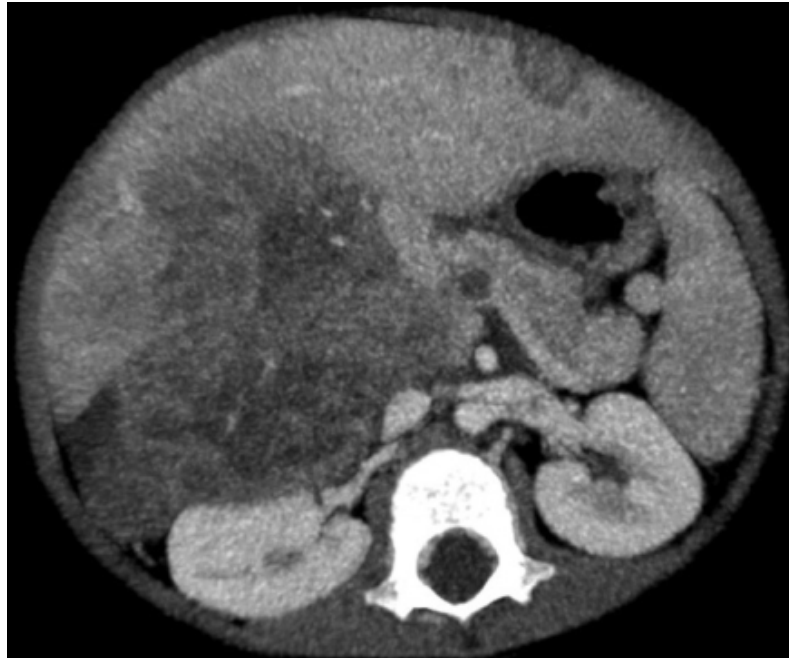
- **PRETEXT III :**  
NO 2 adjoining sections free





# PRETEXT IV

- **PRETEXT IV :**
- No section free of disease



# **Annotation factors changes between 2005 and 2017 PRETEXT classifications**

Roebuck et al, **2005 PRETEXT**  
Ped Radiol 2006

Towbin et al, **2017 PRETEXT**  
Ped Radiol 2018

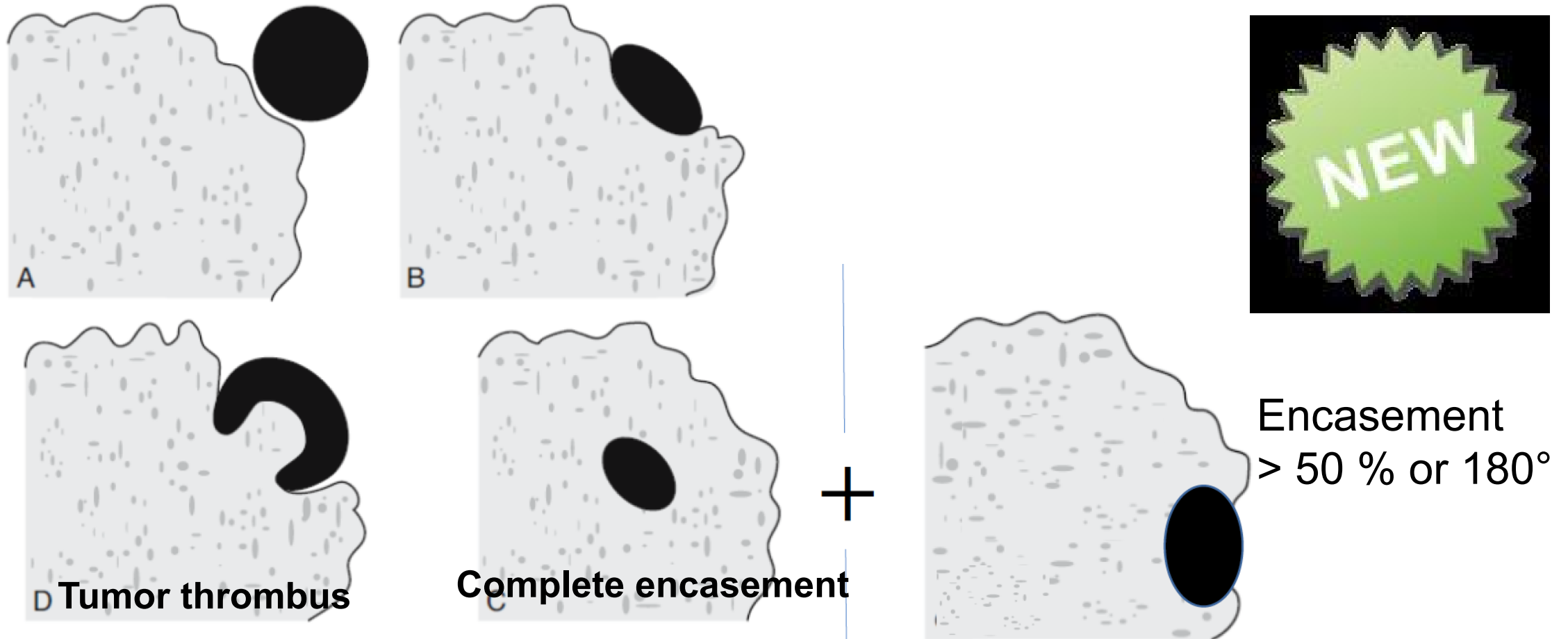
# PRETEXT **Annotation factors**

- Venous extension (V, P)
  - Extrahepatic spread of disease (E)
  - Multifocality (F)
  - Tumour rupture (R)
- 
- Lymph node metastases (N)
  - Distant metastases (M)

# Classification PRETEXT 2017 / 2005

## venous extension : portal P and hepatic V

### First order portal and hepatic veins









# Classification PRETEXT 2017 / 2005

## Venous extension veineuse: portal P and hepatic V

### VASCULAR INVOLVEMENT Baseline only

Tumour >1cm from vein

Tumour <1cm from vein

Tumour encasing >180° and/or obliterating (not effacing) vessel\*

Tumour thrombus

*\*This does not include vessel effacement from mass effect*

Right portal vein	Left portal vein	Main portal vein	Right hepatic vein	Middle hepatic vein	Left hepatic vein	Inferior vena cava
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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P = positive if both orange boxes are checked, or one grey box is checked

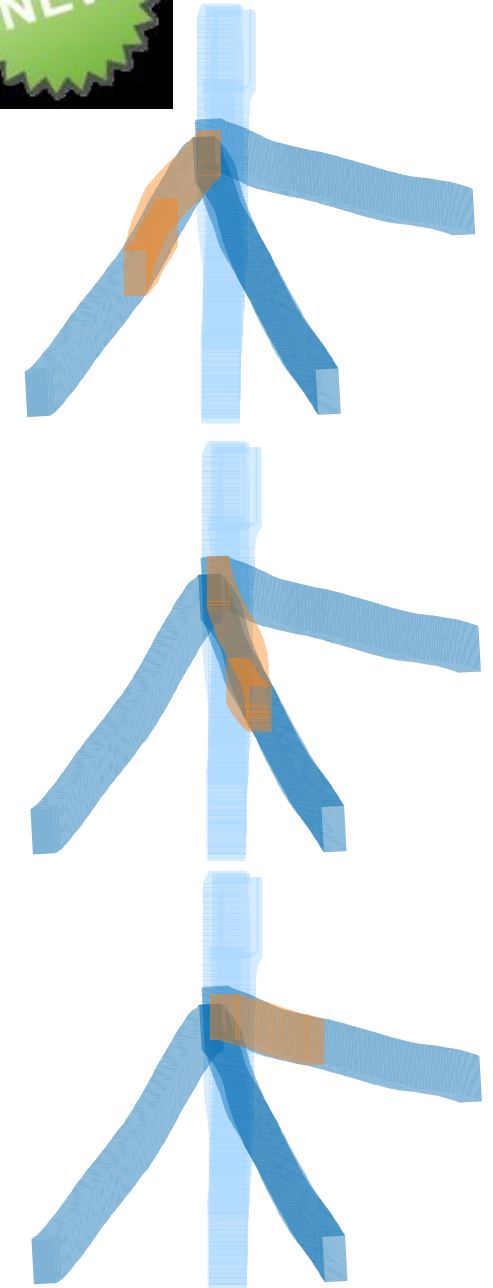
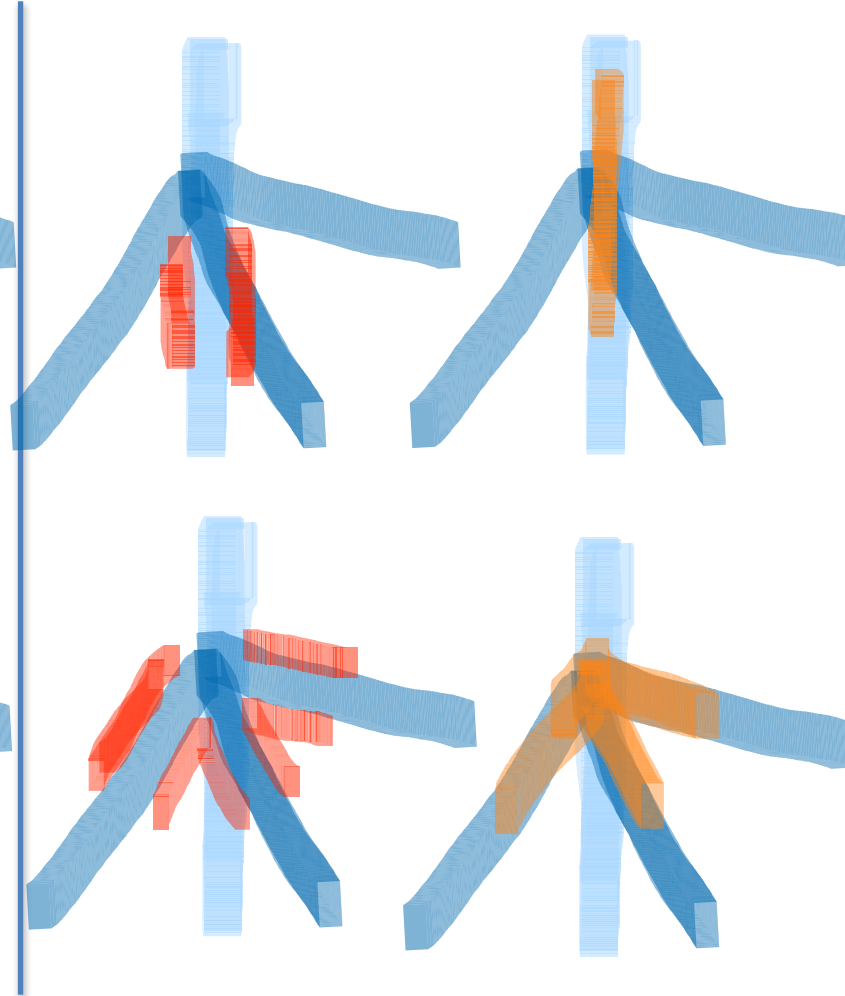
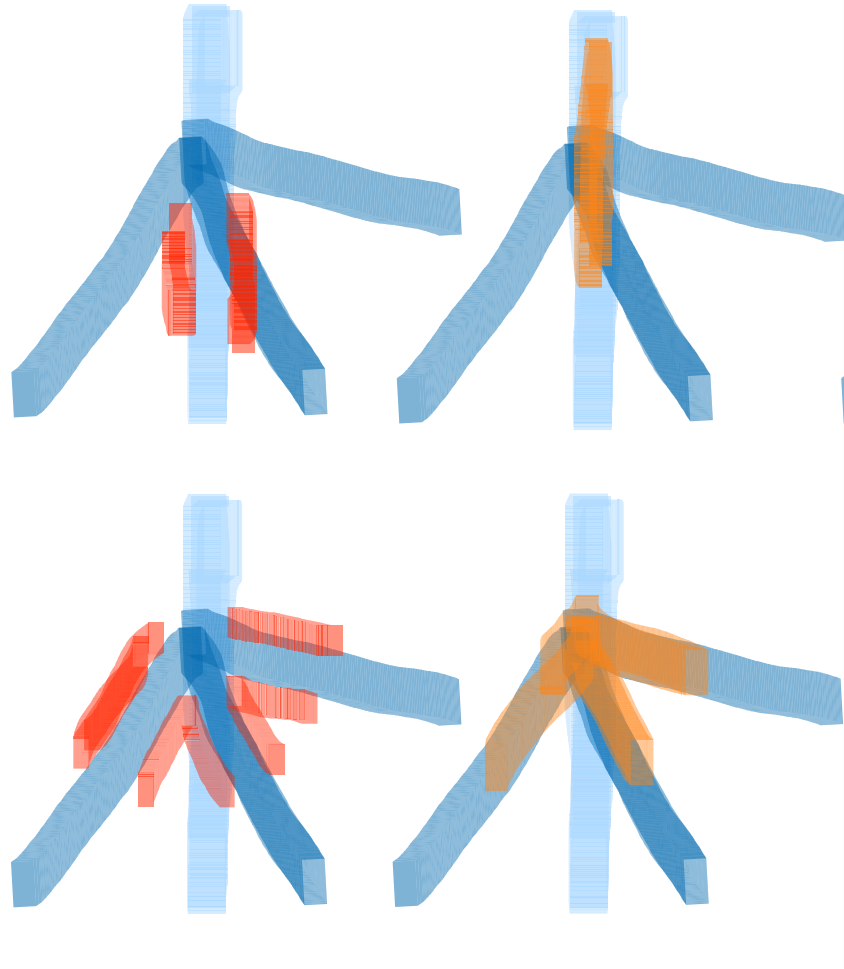
V = positive if both orange boxes are checked, or one grey box is checked

# Classification PRETEXT 2017 vs 2005

Venous extension: hepatic **V** +

2005 (V3, a if thrombus)

2017

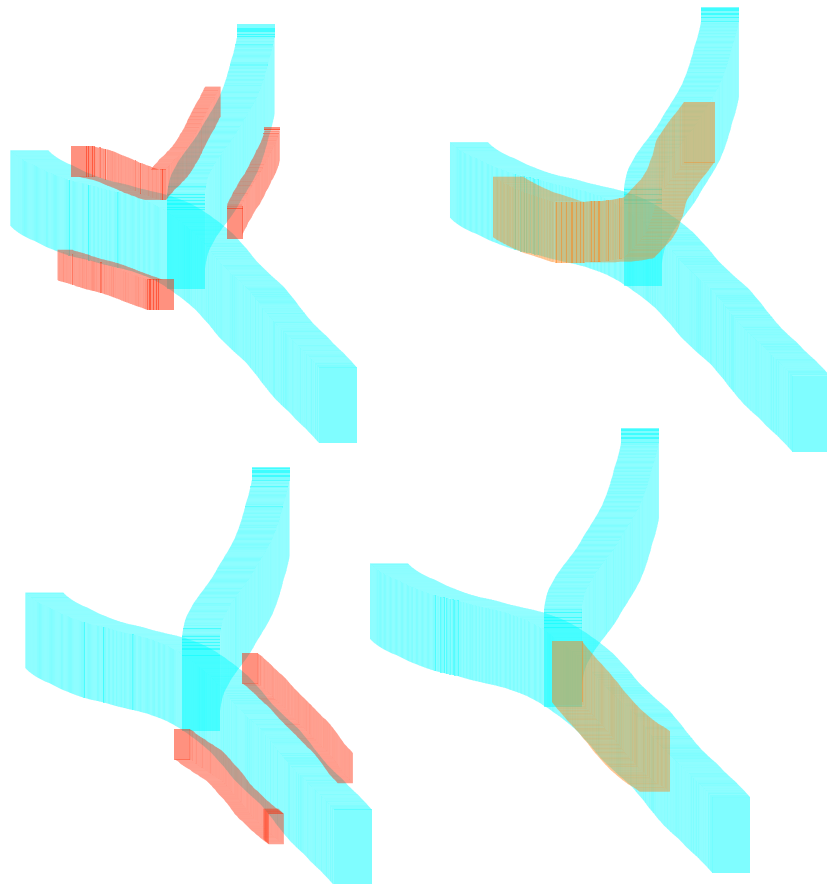


# Classification PRETEXT 2017 vs 2005

Venous extension : **portal P +**



2005: P2 , a (thrombus)



2017



# Classification PRETEXT 2017 / 2005

## Additional criteria: Metastases, lungs+++



### 2005 :

- 1 nodule  $> 10$  mm
- Several nodules  $> 5$  mm

### 2017:

- 1 non calcified nodule  $\geq 5$  mm
- $> 2$  non calcified nodules  $\geq 3$  mm

# Classification PRETEXT 2017 / 2005

## additional criteria: Tumour Rupture R



- **ONLY** based on imaging, *clinical signs are no longer considered*
- **Free fluid in the abdomen or pelvis with one or more of the following findings :**
  - Internal complexity/septations within fluid
  - High density fluid on CT (>25 UH)
  - Imaging characteristics of blood or blood degradation products on MRI
  - Heterogeneous fluid on US with echogenic debris
  - Visible Rupture/hepatic capsular defect on imaging



**Rupture after biopsy or during surgery are not considered as as tumour rupture for the purposes of PRETEXT classification**

# Classification PRETEXT 2017 / 2005

## Additional criteria:

### Extrahepatic spread of disease E



#### 2005:

- E1: direct extension to adjacent structures
- E2: peritoneal nodules
- Prefix a if ascites is present

#### 2017:

- Tumours crosses boundaries /tissues plane
- Tumour is surrounded by normal tissue > 180 °
- Peritoneal nodules present ( > 1 nodule 10 mm or more or > 2 nodules 5 mm or more)

# Classification PRETEXT 2017 / 2005

## Additional criteria: Lymph nodes N



### 2005, N1:

- N+ if short axis > **15 mm**
- N1 if abdominal only
- N2 if extra-abdominal

### • 2017, N+ if:

- Lymph node short axis > **10 mm**
- Porto-caval lymph node > 15 mm
- Spherical lymph node with loss of fatty hilum

# Changes in PRETEXT classification 2017 vs 2005

## possible impacts

### ➤ More V+

- Encasement
- Thrombus in only 1 hepatic vein vs three hepatic veins in 2005

### ➤ More P+

- Encasement
- Thrombus in only 1 portal vein vs both portal branches in 2005

### ➤ More M+

- Smaller cut-off size for metastases 5 vs 10 mm et 3 vs 5 mm



# First preliminary analysis on PHITT cohort

- More Intermediate risk (group C) and less low risk (group B) than expected
- Up-grading linked to annotation factors (P, V, Mets) ?
- = more treatment for some of these patients ?

# SIOPEL Radiology committee

Chair: Helen Woodley, Leeds, UK

## Goals:

Organize national networks for national central reviews

Organize central european review

Optimization of local review by training and teaching files

## Preparation of up-coming PHITT 2 protocol:

- Evaluation and optimization of annotation factors, collaboration with surgical committee +++
- Inclusion of IR techniques for evaluation

Welcome ! Feel free to join us !



Name	Institution
Helen Woodley	Leeds Children's Hospital UK
Stephanie Franchi Abella	Hopital Bicetre Paris France
Simon McGuirk	Birmingham Women's and Children's Hospital UK
Dereck Roebuck	Perth Australia
Philippe Petit	Marseille France
Herve Brisse	Curie Institue Paris Fr
Lilsofie Ording Muller	Oslo University Hopsital Norway
Annemieke Littooj	Utrecht NL
Eirini Katirtzdou	Geneva Switzerland
Sylvianne Hanquinet	University Hospital Geneva Switzerland
Jochen Herrmann	University Medical Center Hamburg Germany
Celine Habre	University Hospital Geneva Switzerland
Anneloes Bohte	Utrecht NL
Co-opted Surgical members	
Carmen Capito (surgical)	
Piotr Czauderna (surgical)	
Katarzyna Sinacka (surgical)	
Geraldine Hery (surgical))	
Florent Guerin?	
Steven Warmann ?	

# European Central review PHITT

Helen Woodley, Simon Mc Guirk, Derek Roebuck, Stéphanie Franchi-Abella

- Group C: understand reasons for upgrading and correct annotation factors
- Focal + mets vs Multifocal +mets
- Presurgical assessment
- Clarification of criteria for diagnosing 'cleared' lung metastases

**Needs representants from every country – Join us !**

**Thank you for your attention !**