

# TIMING OF FETAL DEATH

**Jelena Martinovic-Bouriel**

**Unit of Fetal Pathology**

**APHP-Antoine Béclère Hospital**

**South Paris Medical School**

ASSISTANCE  
PUBLIQUE



HÔPITAUX  
DE PARIS

# FOLLOWING THE FETAL DEATH...

1/ When did the fetal death occur?

2/ Why did the fetus die?

3/ What are the implications for future pregnancies?





# FOLLOWING THE FETAL DEATH...

---

**1/ When did the fetal death occur?**

2/ Why did the fetus die?

3/ What are the implications for future pregnancies?



# OUTLINE

---

- State of the art in the literature
  - Gross criteria
  - Histological criteria
- **Developmental maturational criteria**
  - **Gross: Bone maturation( X-ray)**
  - **Histology : histogenesis (skin, kidneys, lungs)**
- Global approach: few cases
- Algorithm



# IUFD : DEFINITION

---

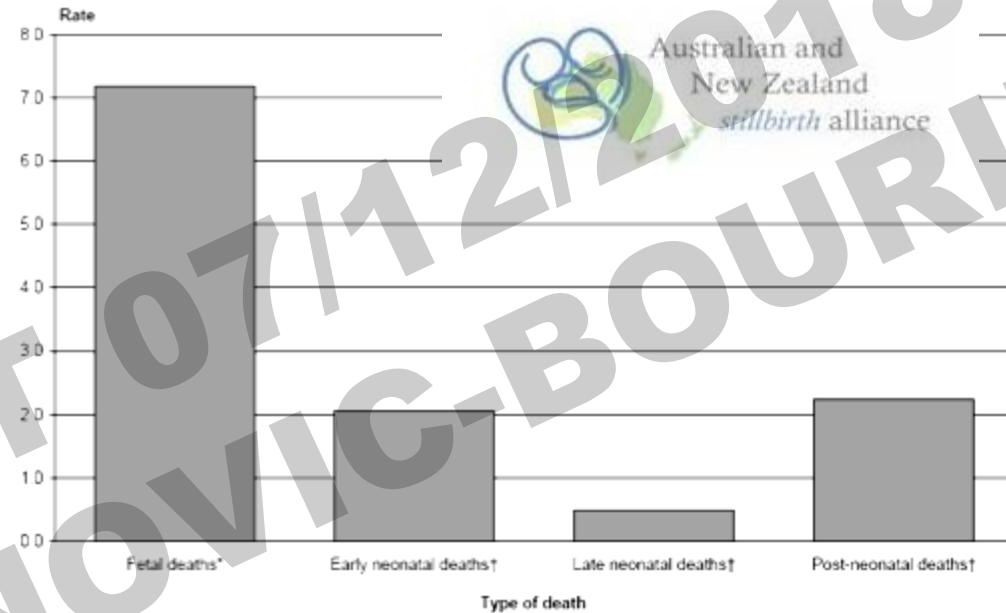
The World Health Organization defines fetal death as follows:

Fetal death is death prior to the complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of pregnancy; the death is indicated by the fact that after such separation the fetus does not breathe or show any other evidence of life such as beating of the heart, pulsation of the umbilical cord or definite movement of voluntary muscles (WHO 1977).



# IUFD : PREVALENCE

Figure 1: Fetal and infant deaths, numbers, total population, 2007



\* = Rate per 1000 total births

† = Rate per 1000 live births

**Gordon et al, (2007). The Lancet**

Stillbirths account for 60% of all deaths during the period roughly defined as starting 20 to 28 weeks prior to birth and 7 to 28 days after birth

# BACKGROUND

## GROSS: Genest & Singer, Obstet Gynecol 1992

- autopsy photographs of 86 stillborns with well-documented time death-delivery (TDD) were studied retrospectively

<u>Gross Features</u>	<u>Time from Death to Delivery at least</u>
Areas of desquamated skin measuring 1 cm or more in diameter	6 <u>hours</u>
Cord discoloration (brown or red)	6 <u>hours</u>
Desquamation involving the skin of the face, back, or abdomen	12 <u>hours</u>
Desquamation of 5% or more of the body surface	18 <u>hours</u>
Desquamation involving 2 or more of the 11 body zones	18 <u>hours</u>
Brown or tan discoloration of the skin, usually involving the abdomen	24 <u>hours</u>
<u>Moderate or severe desquamation</u>	24 <u>hours</u>
<u>Mummification (any)</u>	2 <u>weeks</u>

Body zones are: scalp, face, neck, chest, abdomen, back, arms, hand, leg, foot, and scrotum.

# BACKGROUND

**GROSS: Pauli et al, Am J Med Genet 1994**

<u>Feature</u>	<u>Interval between death and delivery</u>
Skin desquamation of $\geq 1$ cm	$\geq 6$ <u>hours</u>
Skin desquamation involving the face, back and/or abdomen	$\geq 12$ <u>hours</u>
Skin desquamation involving at least 5% of body surface	$\geq 18$ <u>hours</u>
Change of skin coloration to tan or brown	$\geq 24$ <u>hours</u>
<u>Generalized skin desquamation</u>	$\geq 24$ <u>hours</u>
<u>Mummification</u>	$\geq 14$ <u>days</u>



# GROSS: Pauli et al, Am J Med Genet 1994

## 5 STAGES OF FETAL MACERATION:

1. None
2. Slight -- skin slippage, rare bullae, little or no denudation
3. Mild -- focal denudation of multiple regions without other changes
4. Moderate-- generalized skin maceration
5. Advanced -- compression and/or mummification and/or internal liquefaction





# Obstetrics and Gynecology

Volume 80

October 1992

Number 4

Estimating the Time of Death in Stillborn Fetuses: I. Histologic Evaluation of Fetal Organs; an Autopsy Study of 150 Stillborns

DAVID R. GENEST, MD, MICHELLE A. WILLIAMS, ScD, AND  
MICHAEL F. GREENE, MD

# BACKGROUND

## HISTOLOGY : Genest 1992

- 100 stillborn fetuses in the learning set

(« with accurated time of death » = the confirmation that the fetus was alive was followed shortly by clinical constatation that the fetus died »)

→ 23 histological criteria

- 50 test fetuses (blind tests)

→ 10 histol. criteria performed well  
(43/50 - 86%)

# BACKGROUND

## HISTOLOGY: LONB

		<u>detachment</u>	<u>matrix</u> LONB			LONB	LONB	
<u>iver</u>			Individual hepatocyte LONB			Complete LONB		
<u>heart</u>			Inner half of myocardium LONB	Outer half of myocardium LONB				
<u>tract</u>	<u>Mucosal epithelial</u> LONB				<u>Transmural</u> LONB		Complete LONB	
<u>renal</u>			Fetal adrenal cortex LONB		<u>Adult adrenal cortex</u> LONB		Complete LONB	
<u>creas</u>				Complete LONB				

\* Mean time from death – birth : 30h



# BACKGROUND

## PLACENTAL FEATURES?

---

Genest (1992): retrospective evaluation of 36 placentas

- Villous intravascular karyorrhexis ( $\pm 6h$ )
- Vascular lumen abnormalities of stem villi ( $\pm 2d - \pm 2w$ )
- Extensive fibrosis of terminal villi ( $\pm 2w$ )

• Qureshi (2003): retrospective evaluation of 36 placentas of TOPs (TDD : 2,8 – 52h)

- Degeneration of cord smooth muscle
- Intravascular karyorrhexis in villi
- Villous blood vessel luminal abnormalities

\* CANNOT BE USED TO ACCURATELY PREDICT TIME OF DEATH...



# GOLD STANDARDS

## FETAL GROWTH MEASUREMENTS

### EXTERNAL

**Head circumference (HC)**

**Crown-heel length (CH)**

**Foot length (FL)**

X-rays : **Femoral length (FL)**

### INTERNAL

**Visceral weight** (/ fetal weight? age?)

**Intestinal length** (Bryant table in Wigglesworth)

20w : 80+14cm

28w: 184+51cm

40w: 350cm

**Brain morphology** (Larroche, 1978 Atlas )



# ADDITIONAL MARKERS?

---

SOFFOET 07/12/2018  
J. MARTINOVIC-BOURIEL



# ADDITIONAL MARKERS

---

Developmental maturational criteria:

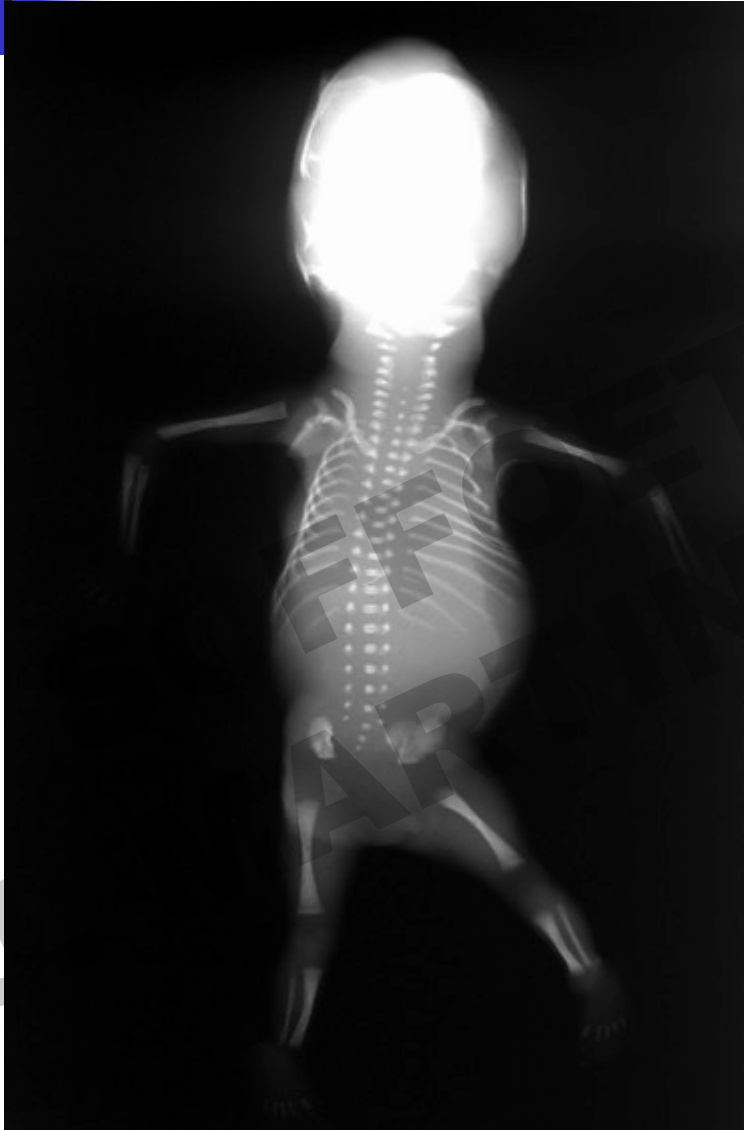
Gross: Bone maturation( X-ray)

Histology : histogenesis (skin, lungs, kidneys)

SOPHIE 07/12/2018  
J. MARTINOVIC BOURIEL



# NORMAL FETAL BONE MATURATION



16 weeks :

- \* Vertebral bodies are visibles (C3 - S3)
- \* Squared iliac bones

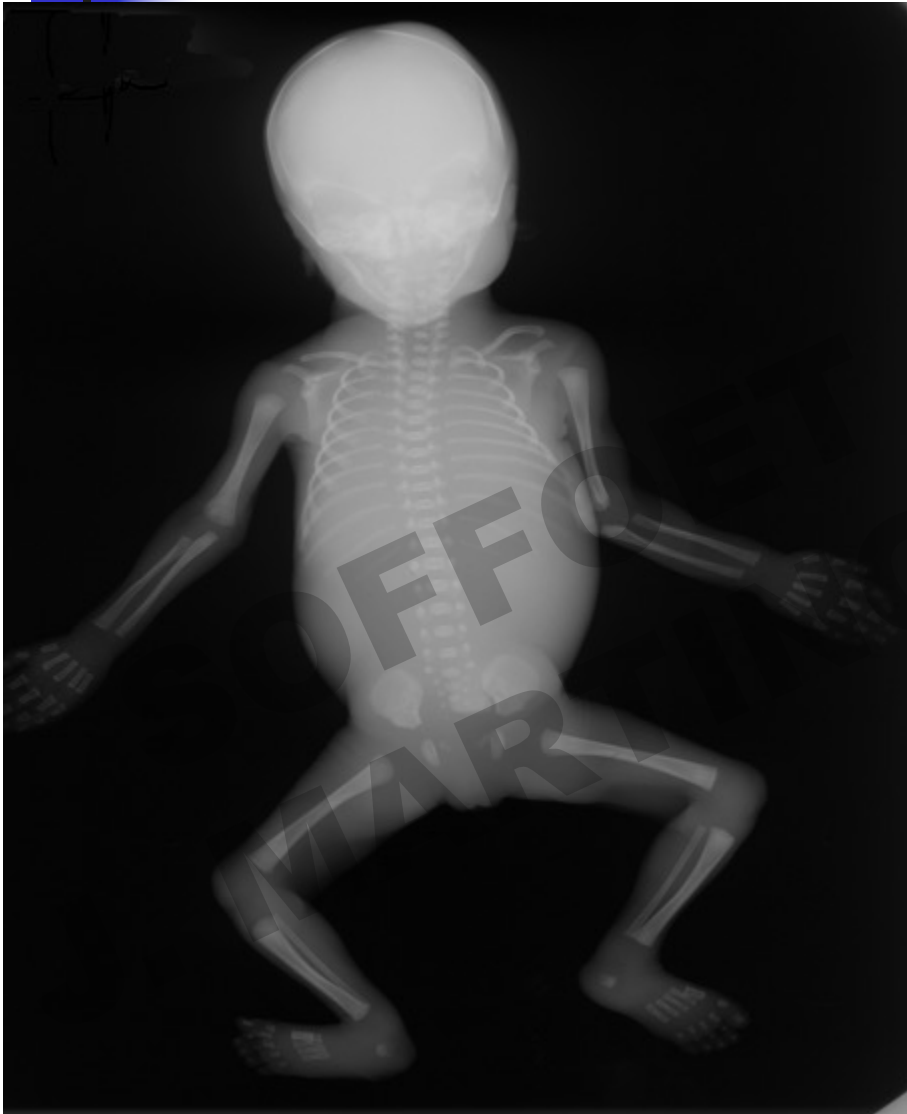
# NORMAL FETAL BONE MATURATION



17 weeks :

- \* Convexity of superior ulnar part
- \* Ossified 2<sup>nd</sup> hand phalanges, (5<sup>th</sup> rounded)
- \* Visible ischial bones

# NORMAL FETAL BONE MATURATION



23S weeks :

- \* Complete ossification of vertebral bodies (-S4)
- \* Vertical ischial bones
- \* Visible pubic bones
- \* Calcaneum present

# NORMAL FETAL BONE MATURATION



27 weeks :

- \* S5 ossified
- \* Concave ischial bones
- \* Pubic bones well-developed
- \* Round calcaneum
- \* Apparent astragals

# NORMAL FETAL BONE MATURATION



32 weeks :

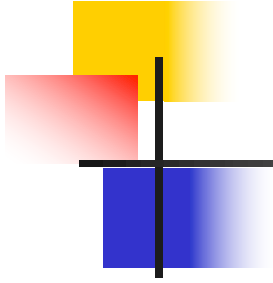
- \* Calcaneum & astragal well-developed
- \* Sharp margins of pubic bones

# NORMAL FETAL BONE MATURATION



36 weeks :

- \* Inferior femoral ossif. Point (Beclard) & superior tibial ossif.point (Todt) are visibles
- \* Visible sternum
- \*Ossified coccyx

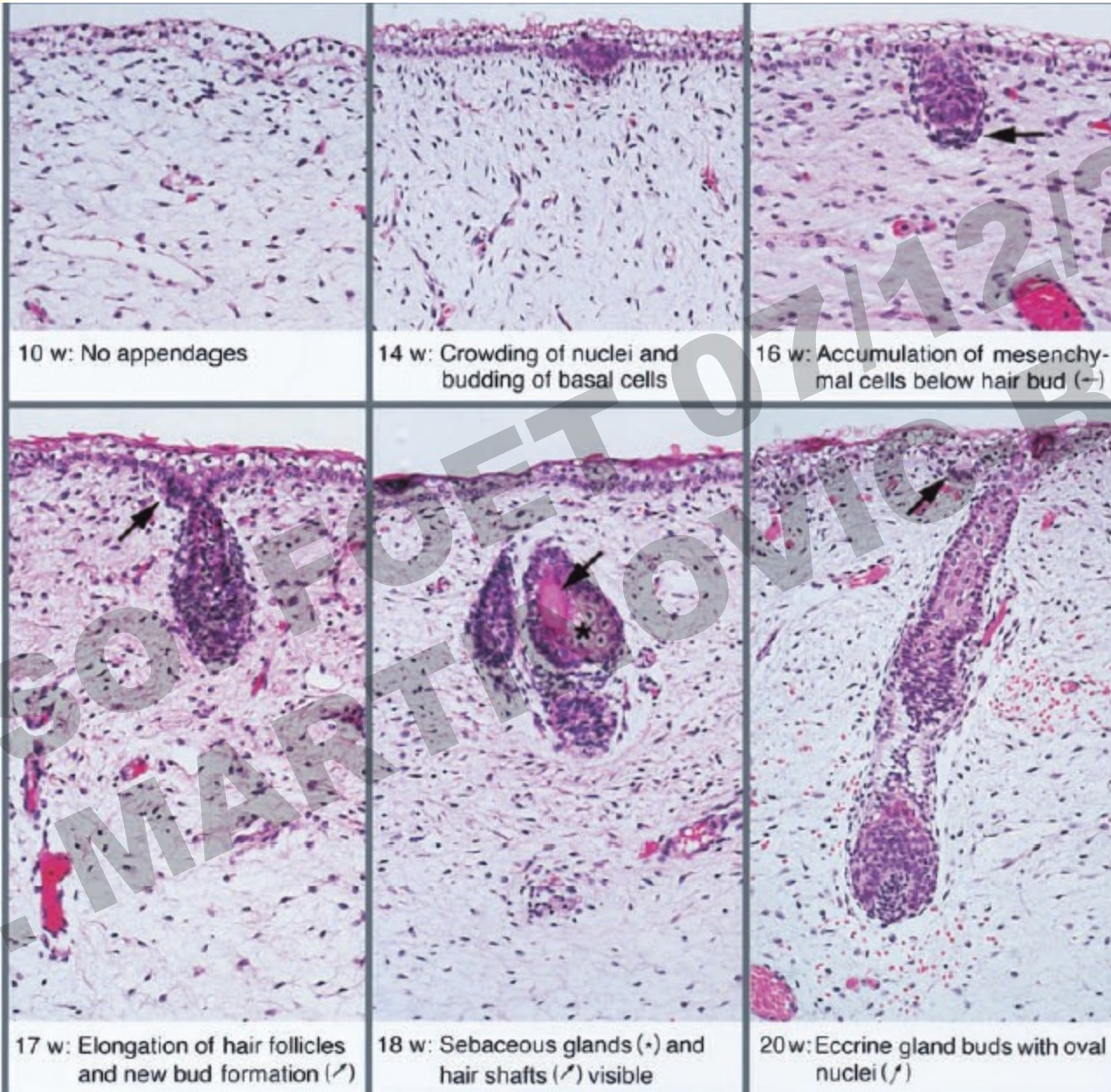


# **HISTOGENESIS MARKER: FETAL SKIN**

SOFFOET 07/12/2018  
J. MARTINOVIC-BOURIEL



# HISTOGENESIS MARKER: FETAL SKIN

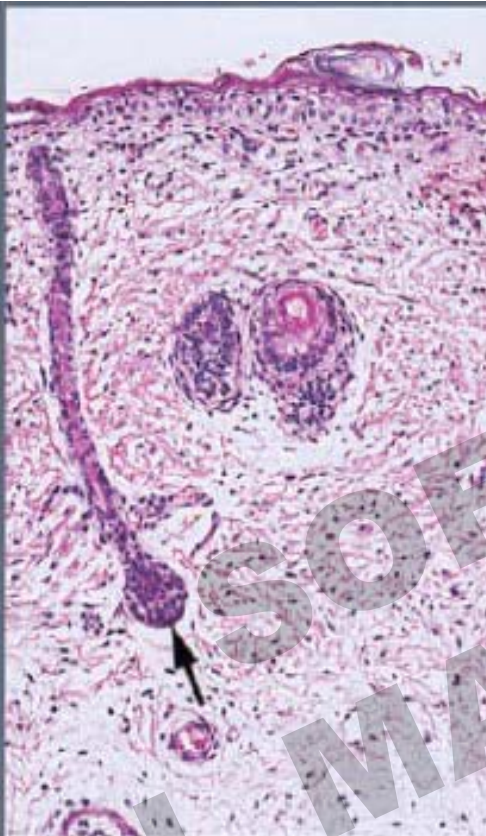
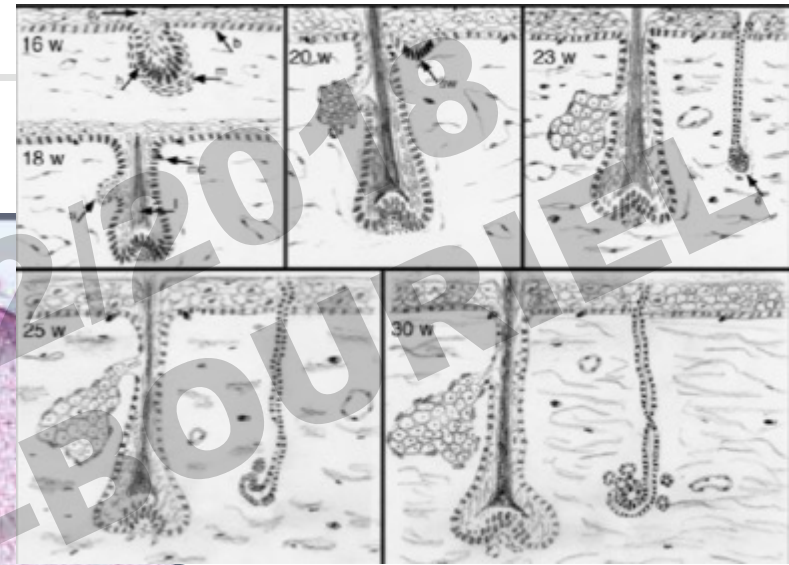


Ersch & Stallmach, 1999

- Abdominal skin sampling



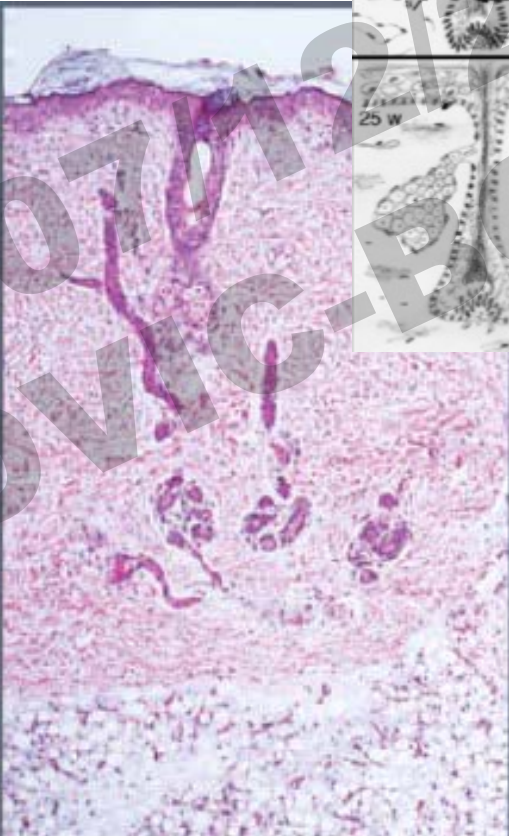
# HISTOGENESIS: SKIN



23 w: Elongation of mostly solid eccrine ducts (\)

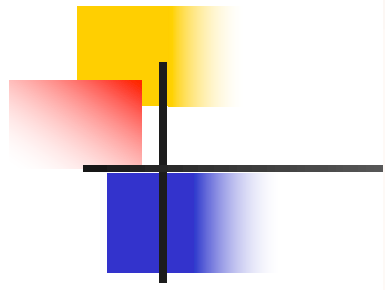


25 w: Early coiling of eccrine ducts with lumen (/)

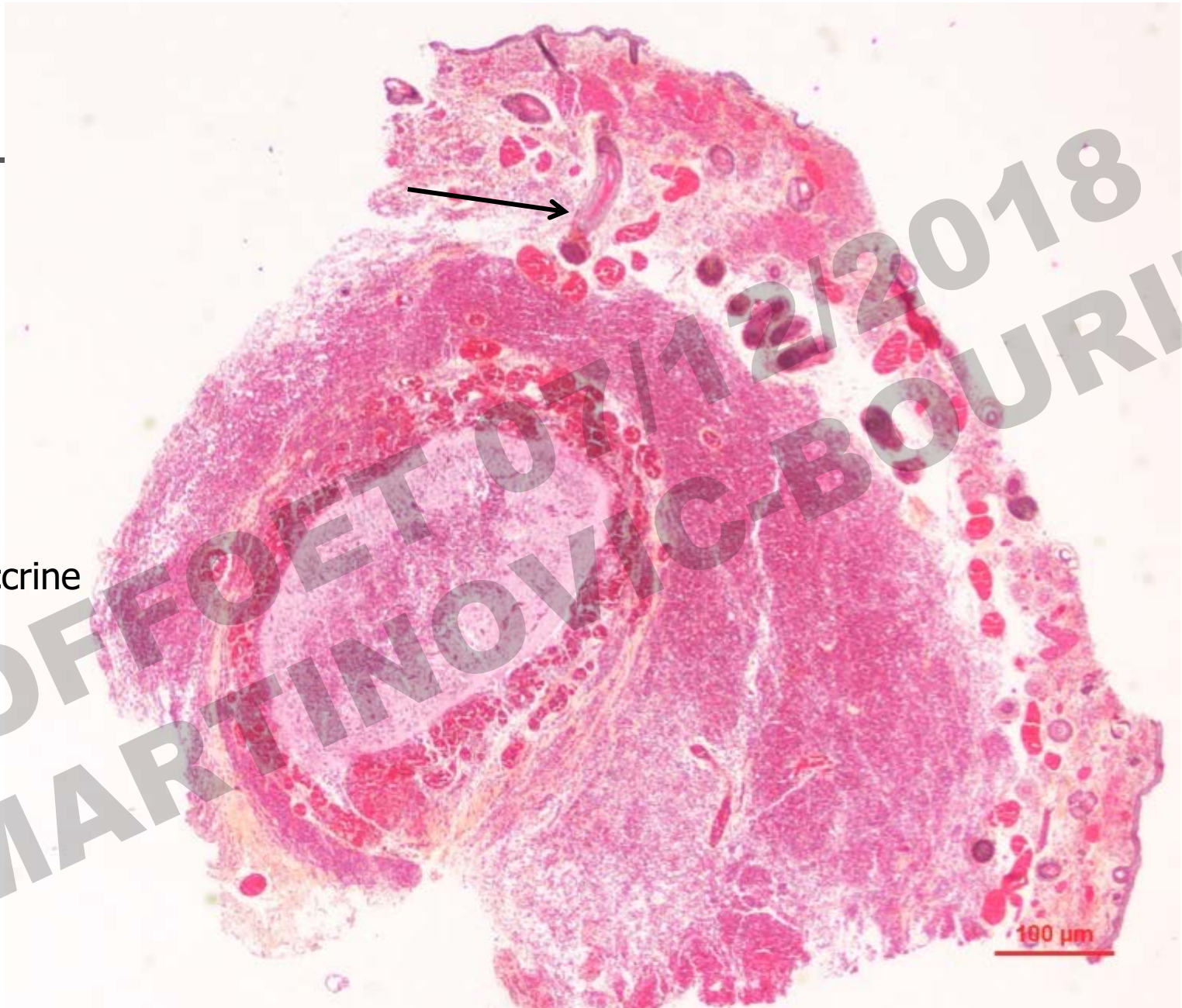


30 w: Coiling of eccrine glands seen as multiple transverse sections





Fetus 24w:  
Elongation of eccrine  
ducts



SOFFOET 07/12/2018  
J. MARTINOVIC-BOURIEL

\*CD : Histogenesis of the skin (embryo & fetus)



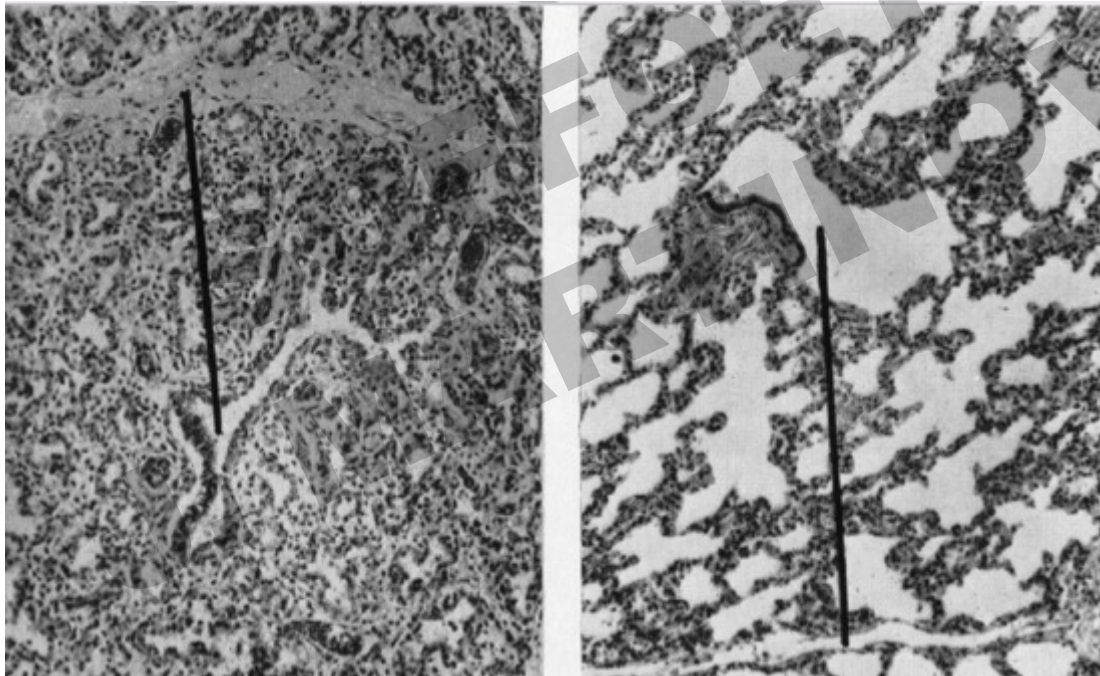
---

# **HISTOGENESIS : LUNGS**

SOFFOLET 07/12/2018  
J. MARTINOVIC BOURIEL

# LUNG HISTOGENESIS : RADIAL ALVEOLAR COUNT (CRA)

concept of the terminal respiratory unit of the lung :  
mass of air spaces distal to a terminal respiratory bronchiole

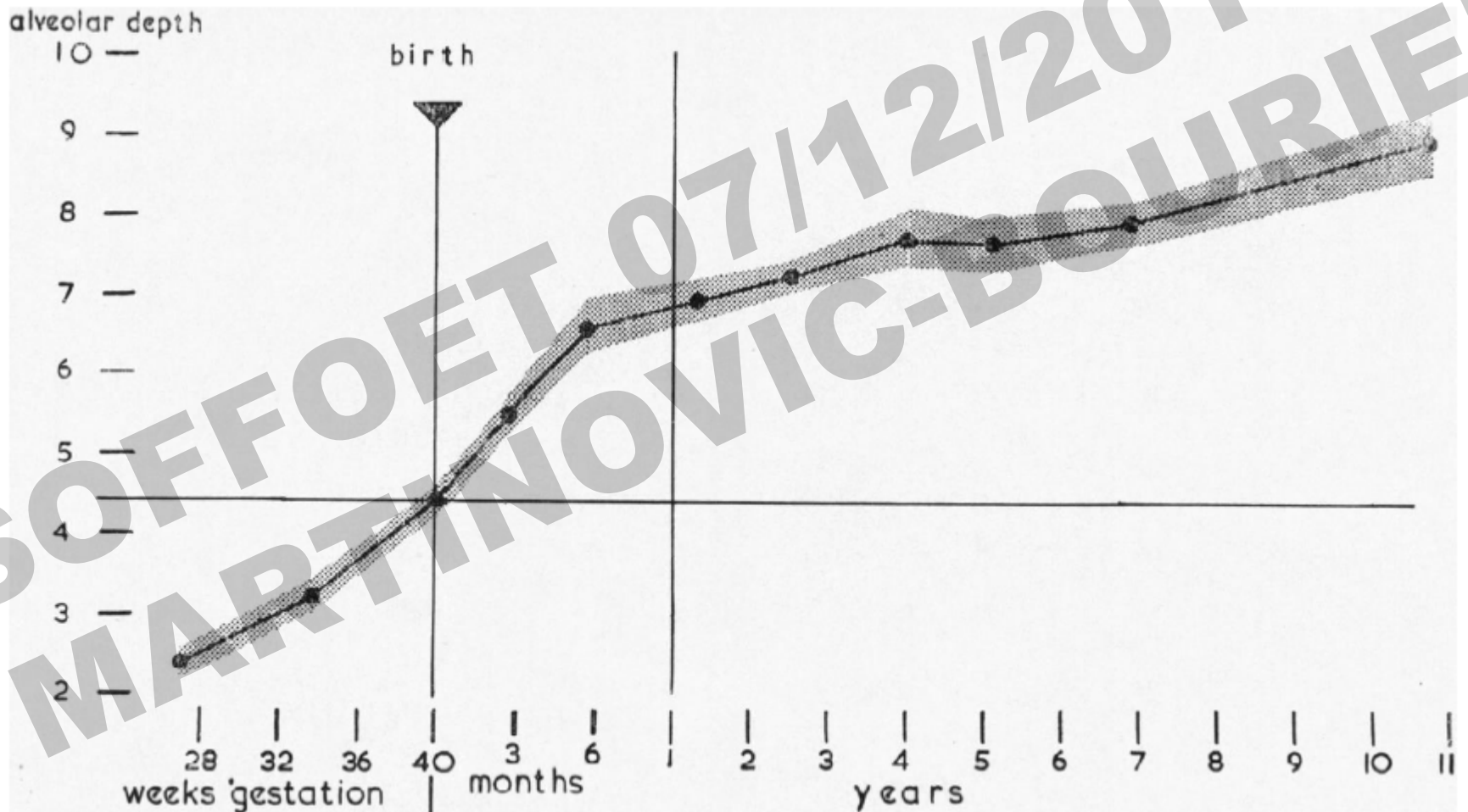


24-27w	2,2
28-31w	2,6
32-35w	3,2
36-39w	3,9
40w	4,4
D1-D30	5,5



# LUNG HISTOGENESIS : RADIAL ALVEOLAR COUNT (CRA)

*ARCHIVES OF DISEASE IN CHILDHOOD*





---

# **HISTOGENESIS : FETAL KIDNEYS**

SOFFOLET 07/12/2018  
J. MARTINOVIC-BOURIEL

# RENAL HISTOGENESIS

- Evaluation of the total n° of nephron generations:
  - **Medullary ray glomerular counting (Hinchliffe SA)**

## Immature glomeruli counting (Potter)

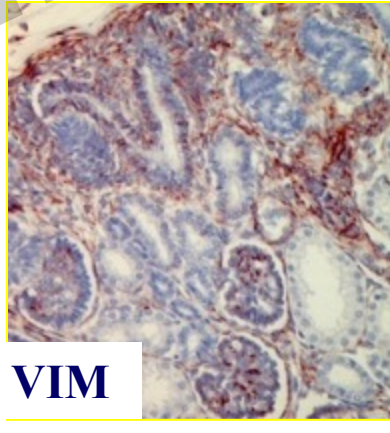
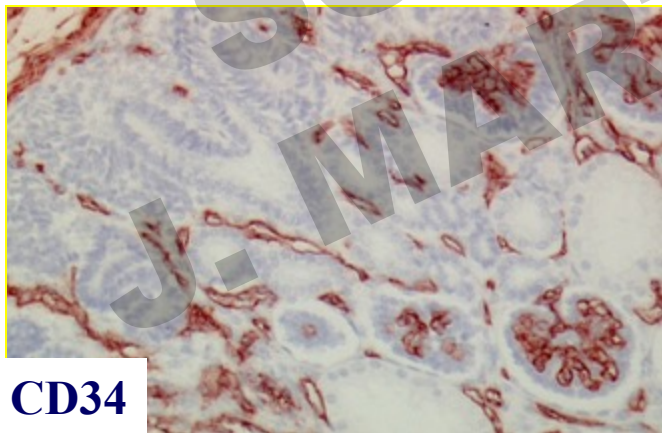
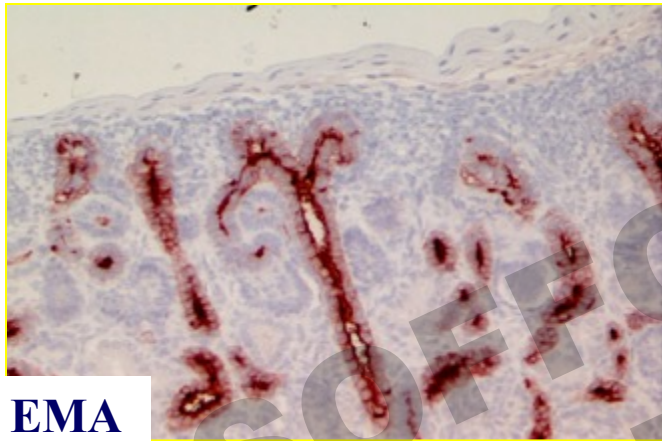
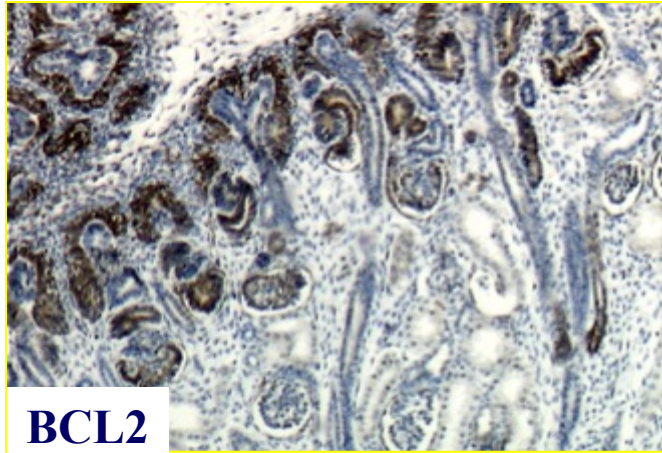
27w : blastema  
28w : 3 layers  
32w : 2 layers  
36w : 1 layer  
40w : 0

## Mature glomeruli counting (Dorovini-Zis, in Wigglesworth)

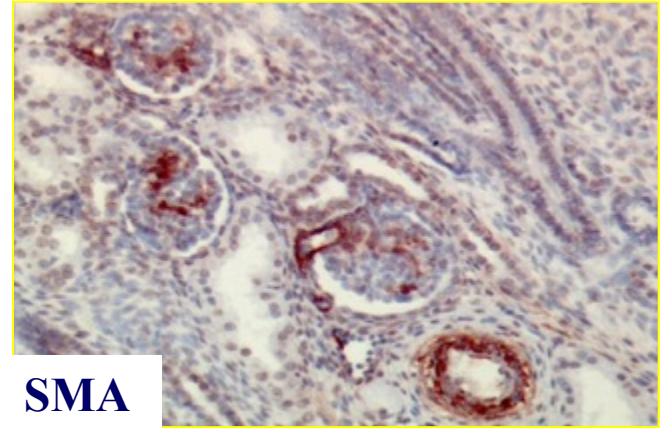
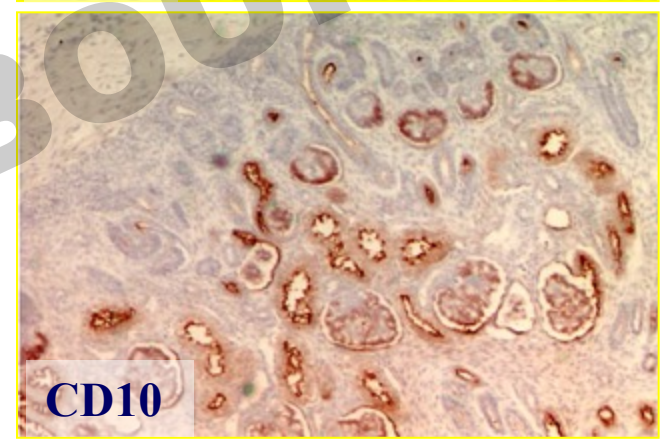
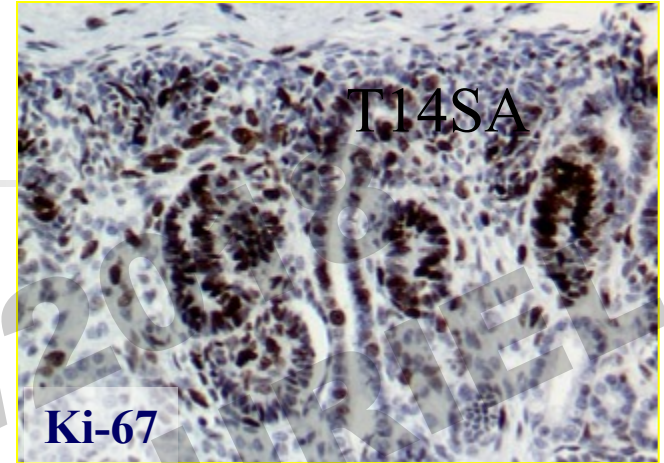
16-23w : 3 layers  
24w : 4+1  
25w : 5+1  
26w : 6+1  
27w : 7+1  
28w : 8+1  
29w : 9+1  
30w : 10+1  
32w : 12+1  
33w : 13+1  
34w : 14+1



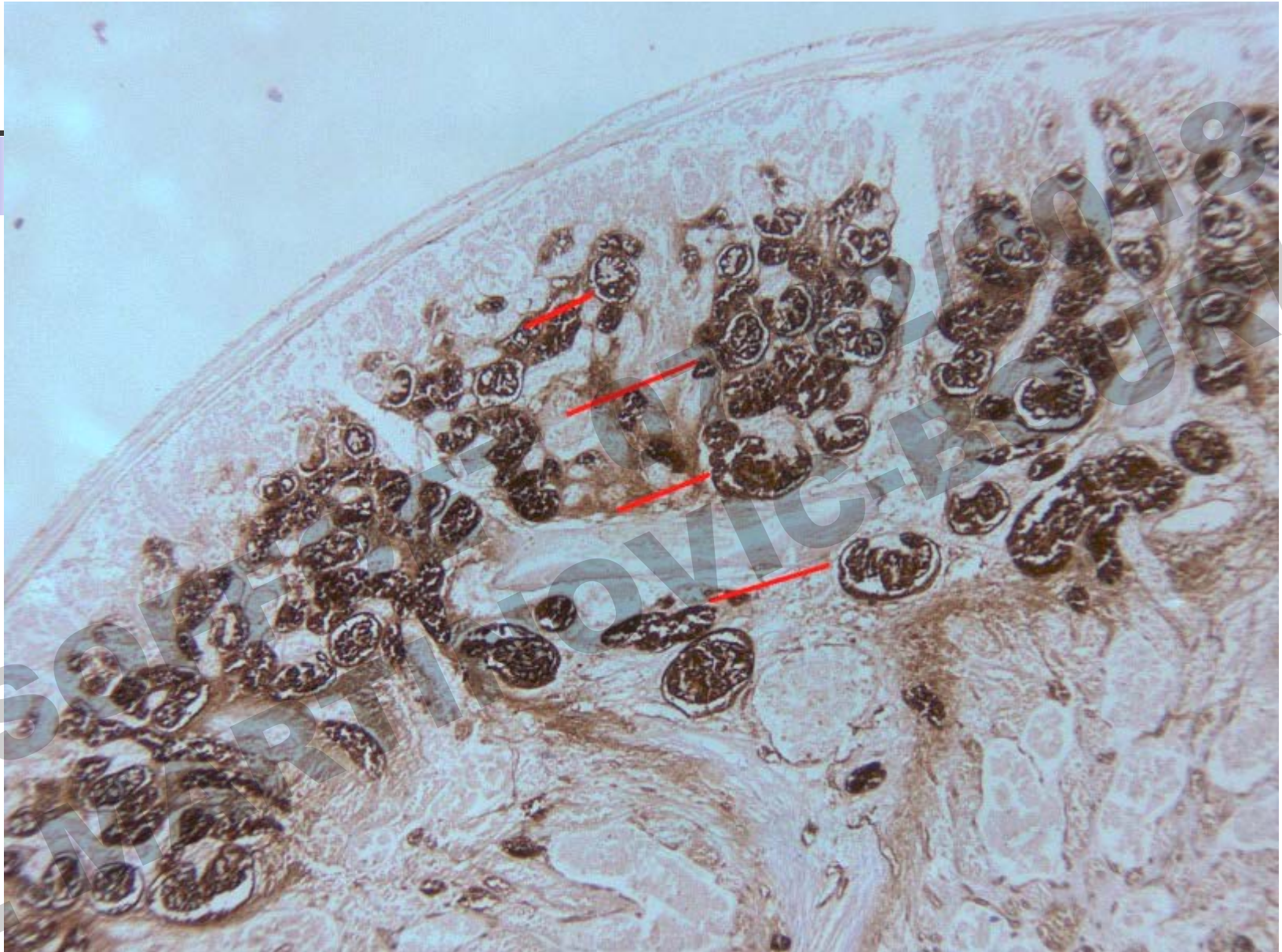




**CONTROL  
(14w)**







Macerated fetus: corresponding to 24w of renal maturation

# CASE 1

IUFD @21,3w, G3P2 , 35yo

BW: 129g; CH: 21,5cm, HC: 13cm, FL: 2cm

17/18 weeks (= 3-4,3 weeks retention)

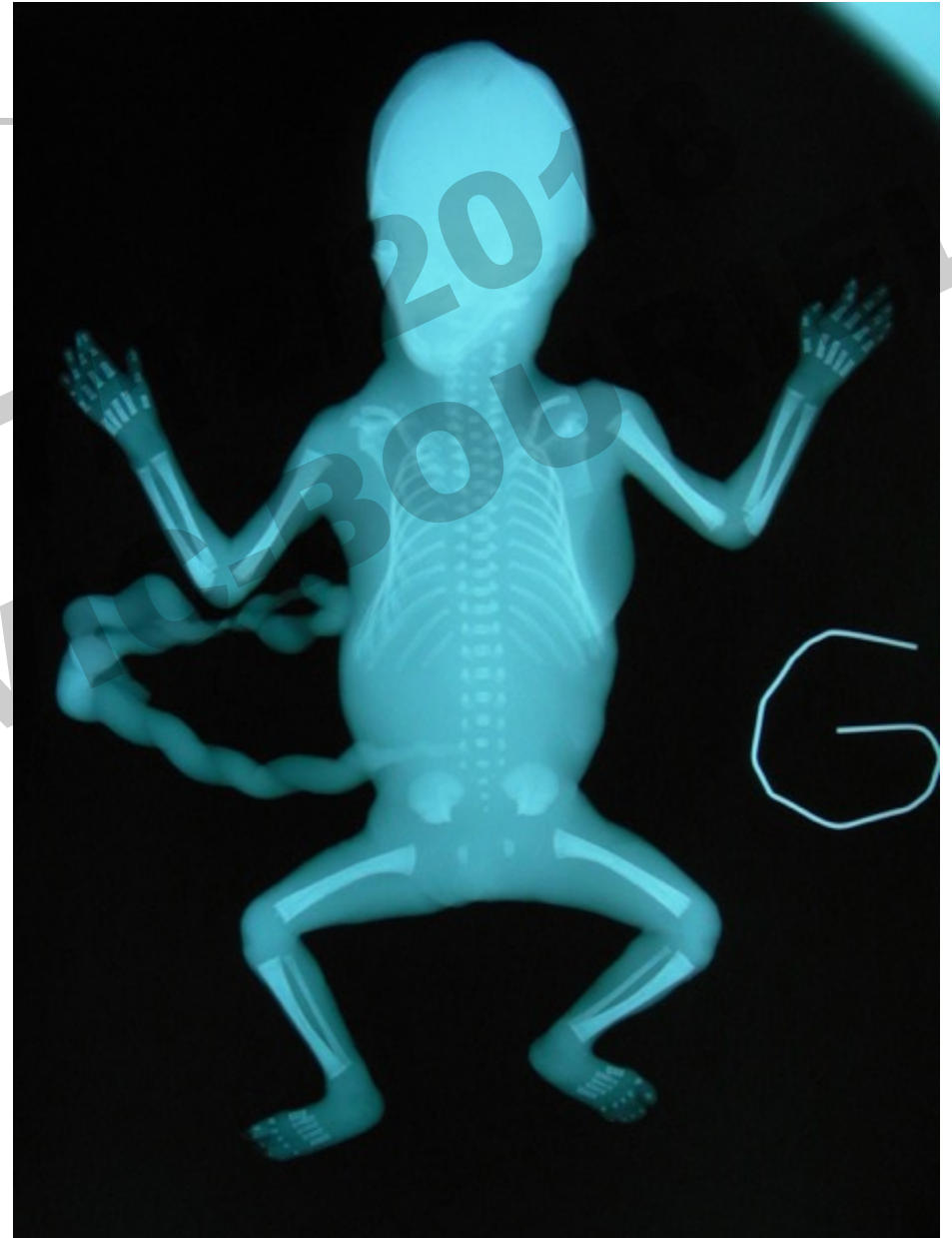
Stage of mummification = + 14 days



# CASE 1 : X-rays

FL (27 mm) : 17w

Bone maturation : 17w



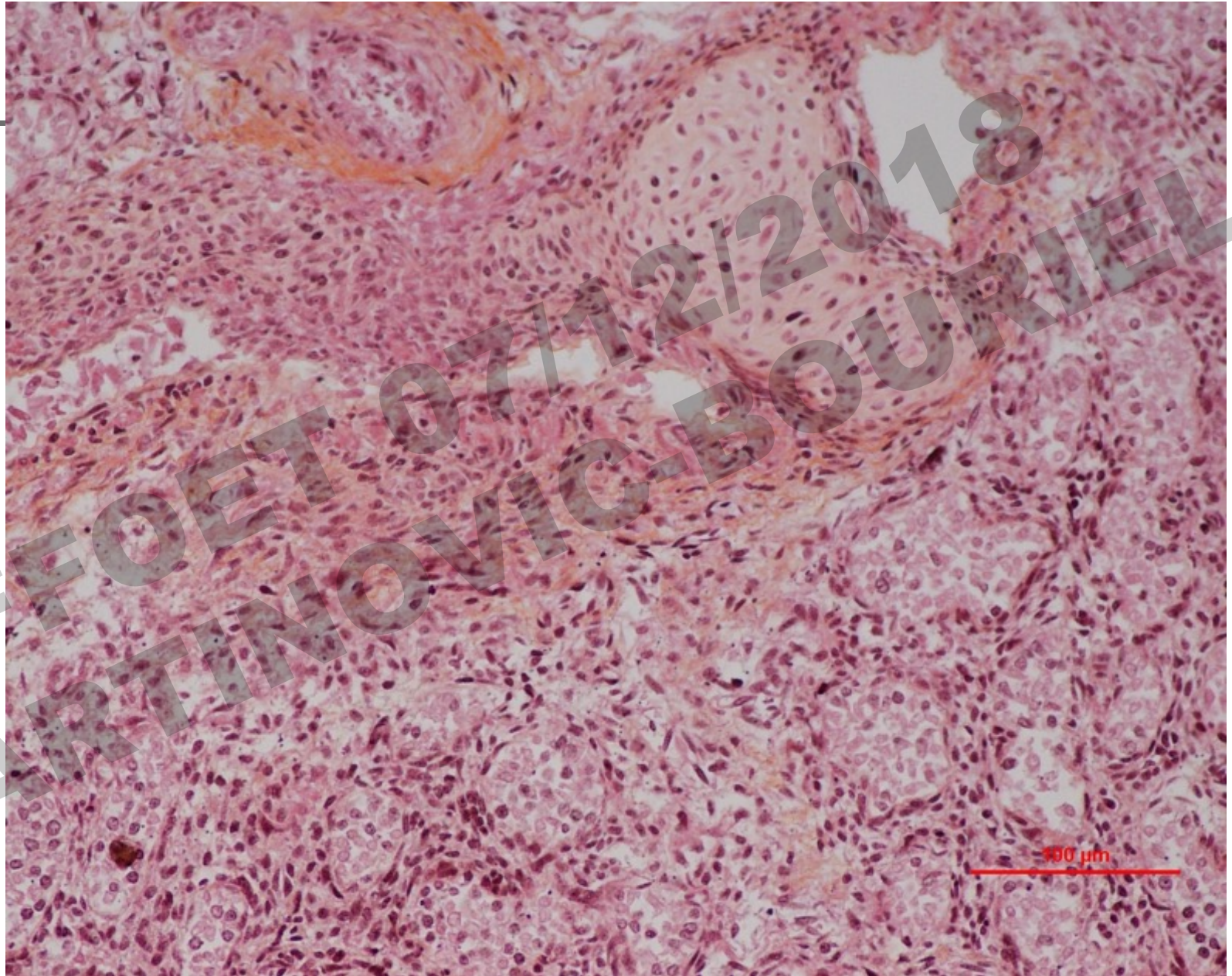




# LUNG

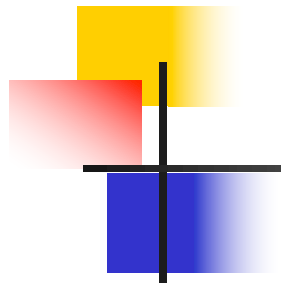
Tracheal cartilage &  
alveolar wall LONB:

± 2 weeks

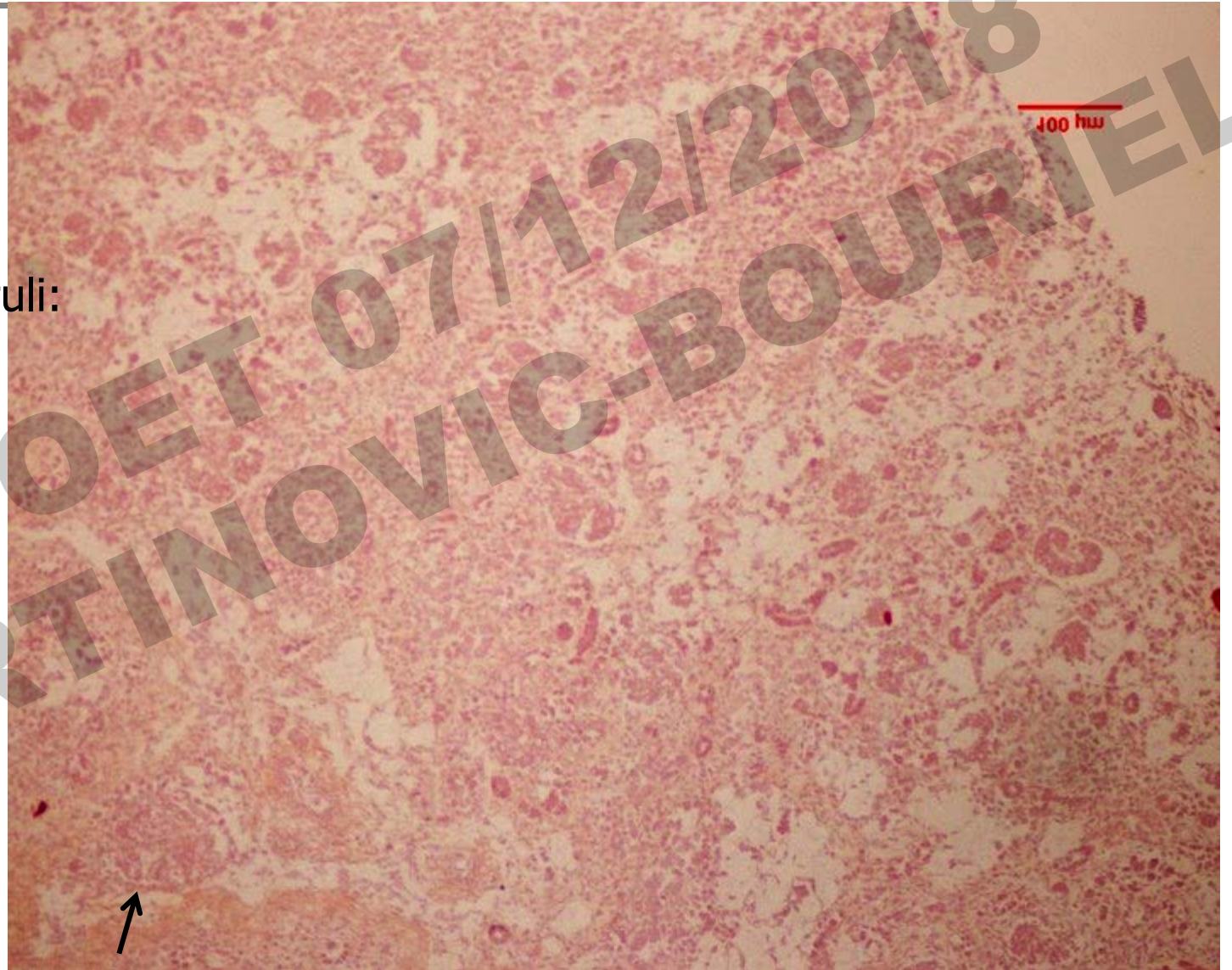




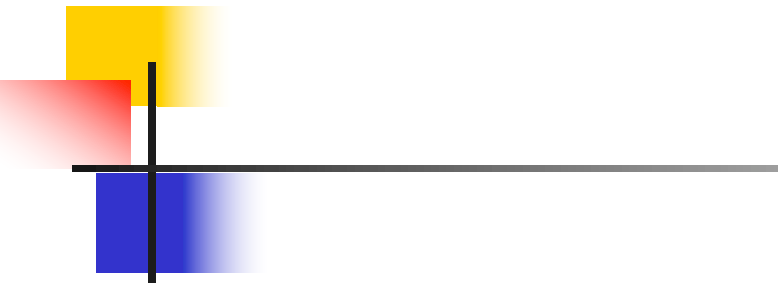
# CASE 1: KIDNEY



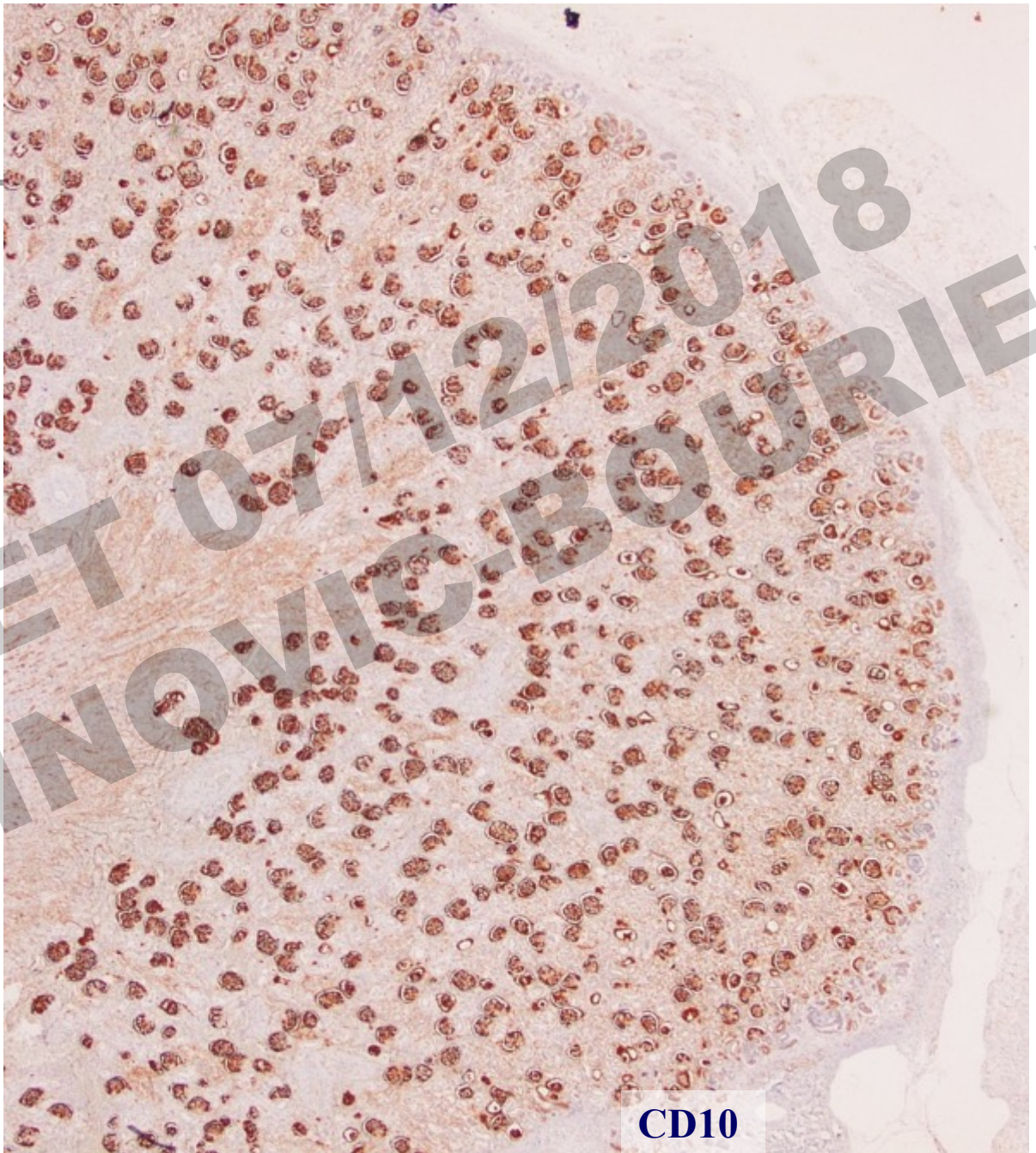
3 layers of mature glomeruli:  
16-17 weeks







Stillborn : 13 layers  
of mature glomeruli  
corr to 33w of renal  
maturation



CD10

# CASE 1

Fetal growth measurements :  
**17/18weeks**

Stage of mummification = + 14 days

X-rays concordance

**Bone maturation 17 w**

Histology:

**Renal maturation 16-17w**

**Approx. 4 weeks of retention**



## CASE 2

IUFD @18w, G6P2 , 36yo

BW: 83g; CH: 16,5cm, HC: 11cm, FL: 1,8cm

→ 15/16weeks = 14 – 21 days

Stage of mummification = + 14 days





## CASE 2: X-rays

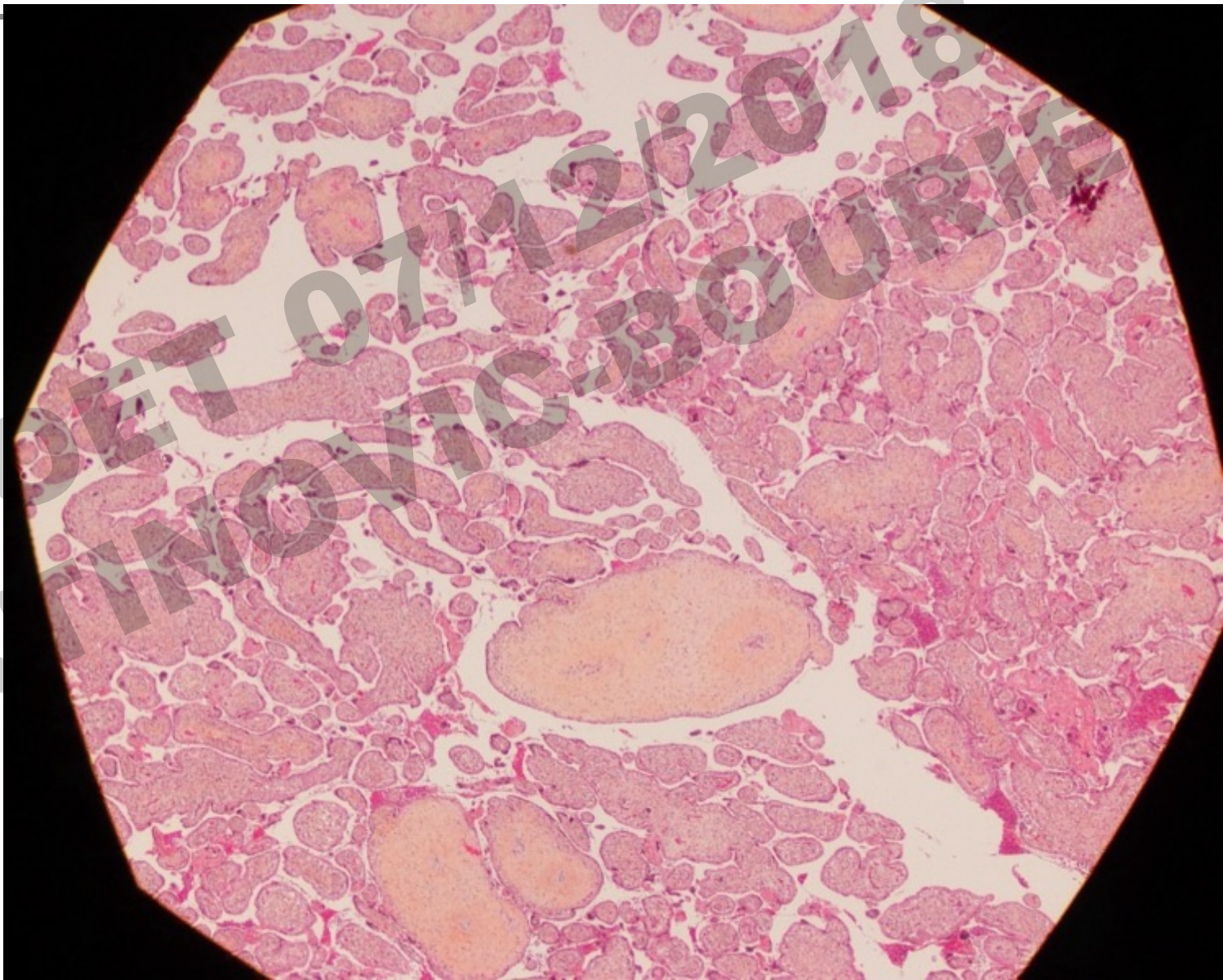
FL (18mm) : 15w

**Bone maturation : 17w**



# PLACENTA

\* non informative





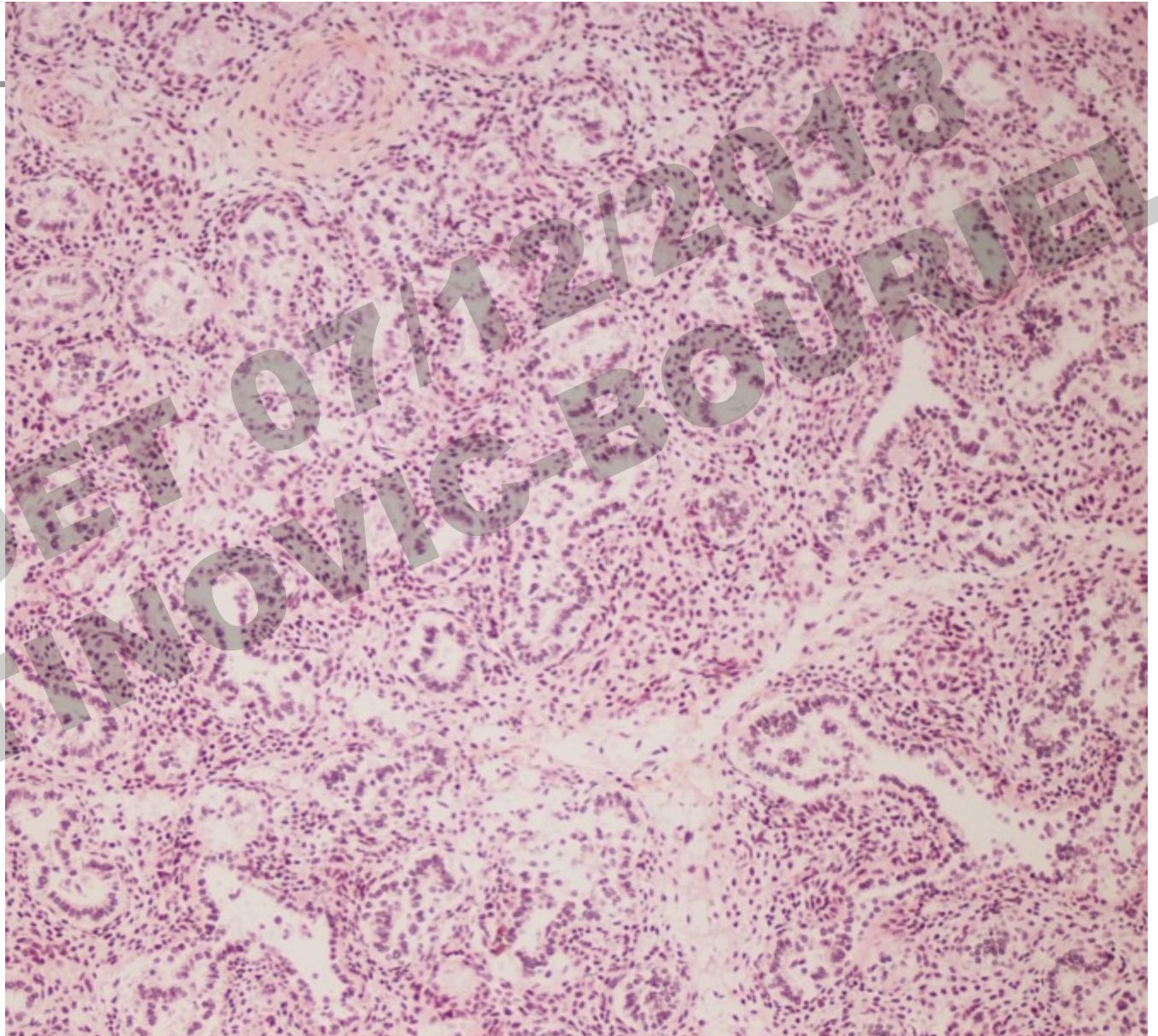
# LUNGS

Histological criteria :

1/ glandular stage

2/ epithelial detachments  
+ LONB

→ + 2 weeks

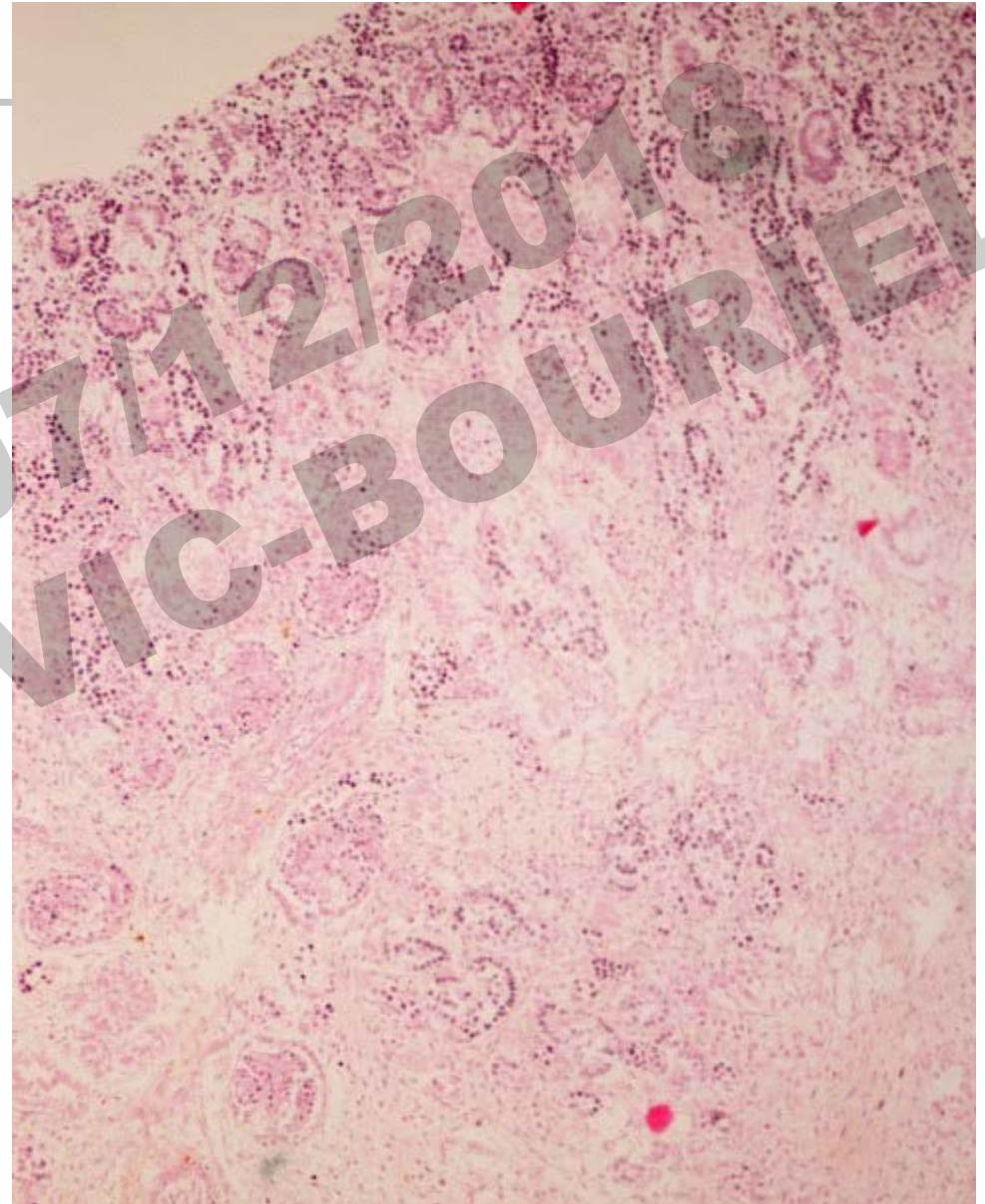




# KIDNEY

## Histological criteria:

- 3 layers of mature glomeruli  
16-17w
- Glomerular LONB
- 48h – 4 weeks





## CASE 2

Fetal growth measurements :

➔ 15/16weeks

Stage of mummification = + 14 days

X-ray discordance = IUGR

Bone maturation ➔ 17 w

Histology:

Renal maturation ➔ 16-17w

Approx. 1-2 weeks of retention



## CASE 3

IUFD @24,4w, 27yo

BW: 562g; CH: 31cm, HC: 21cm, FL: 4,3cm

→ 24w (96h)

Brown discoloration of the skin = + 24h (-2w)





## CASE 3 : X-rays

FL (42mm) : 23w

**Bone maturation : 24w**

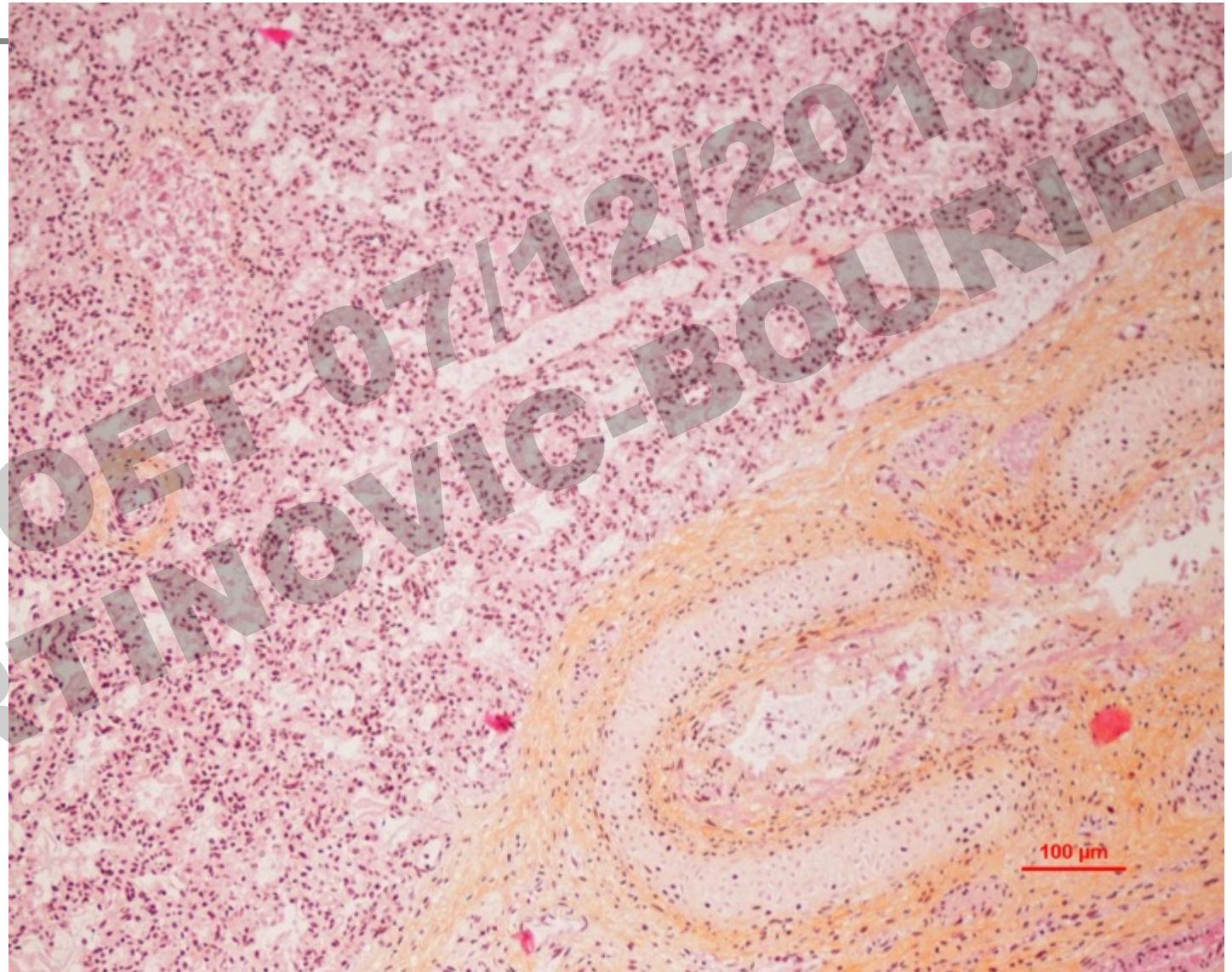
SOFFOET  
J. MARTINO





# LUNG

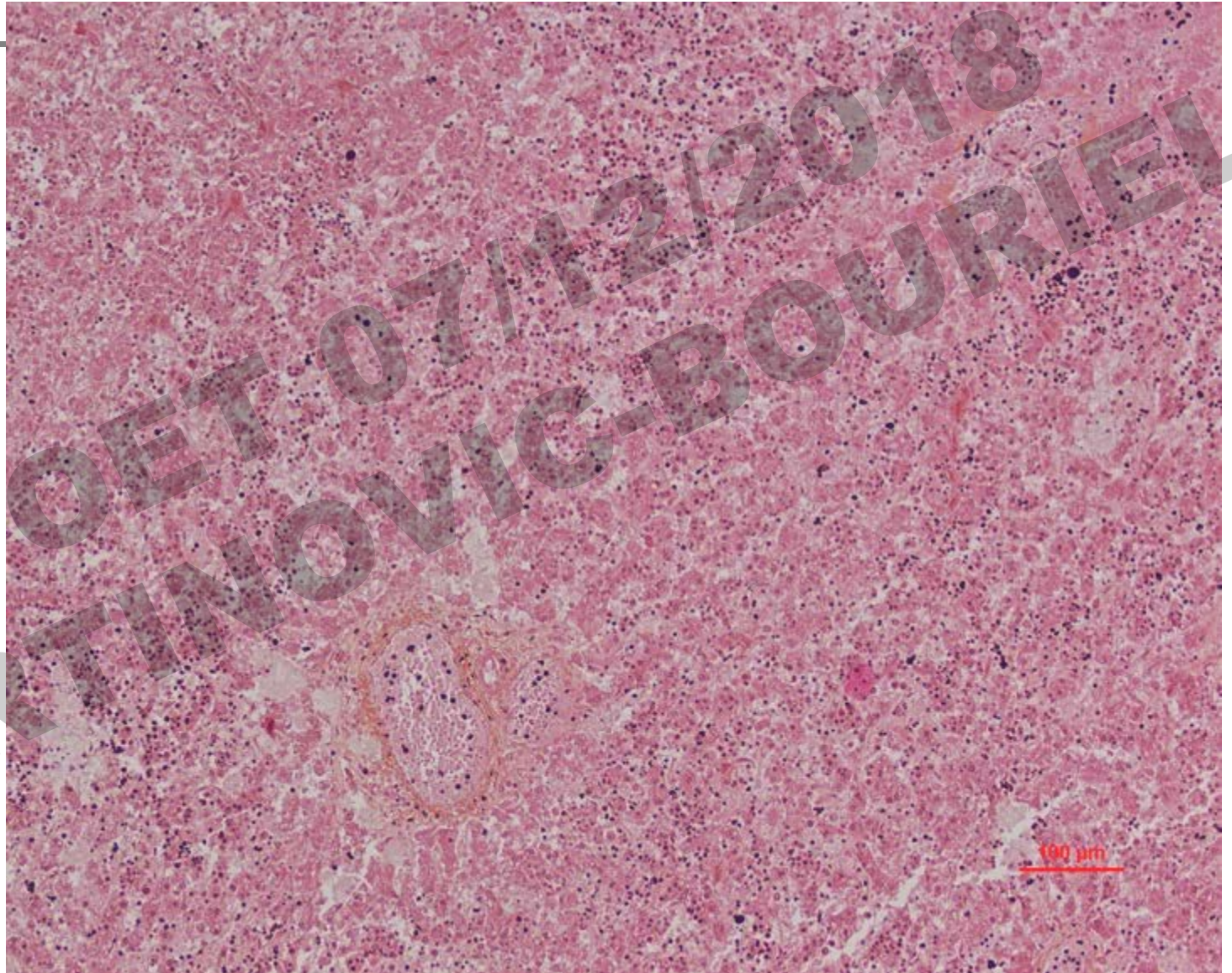
Bronchial cartilage  
matrix LONB:  
24-96h



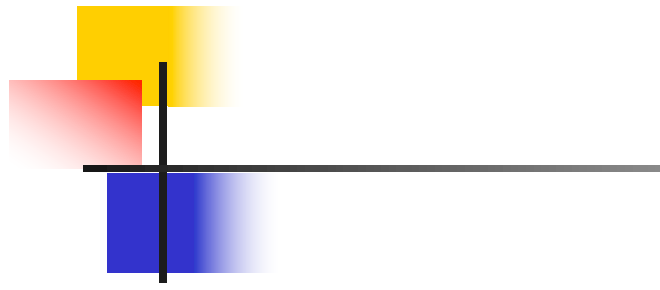


# LIVER

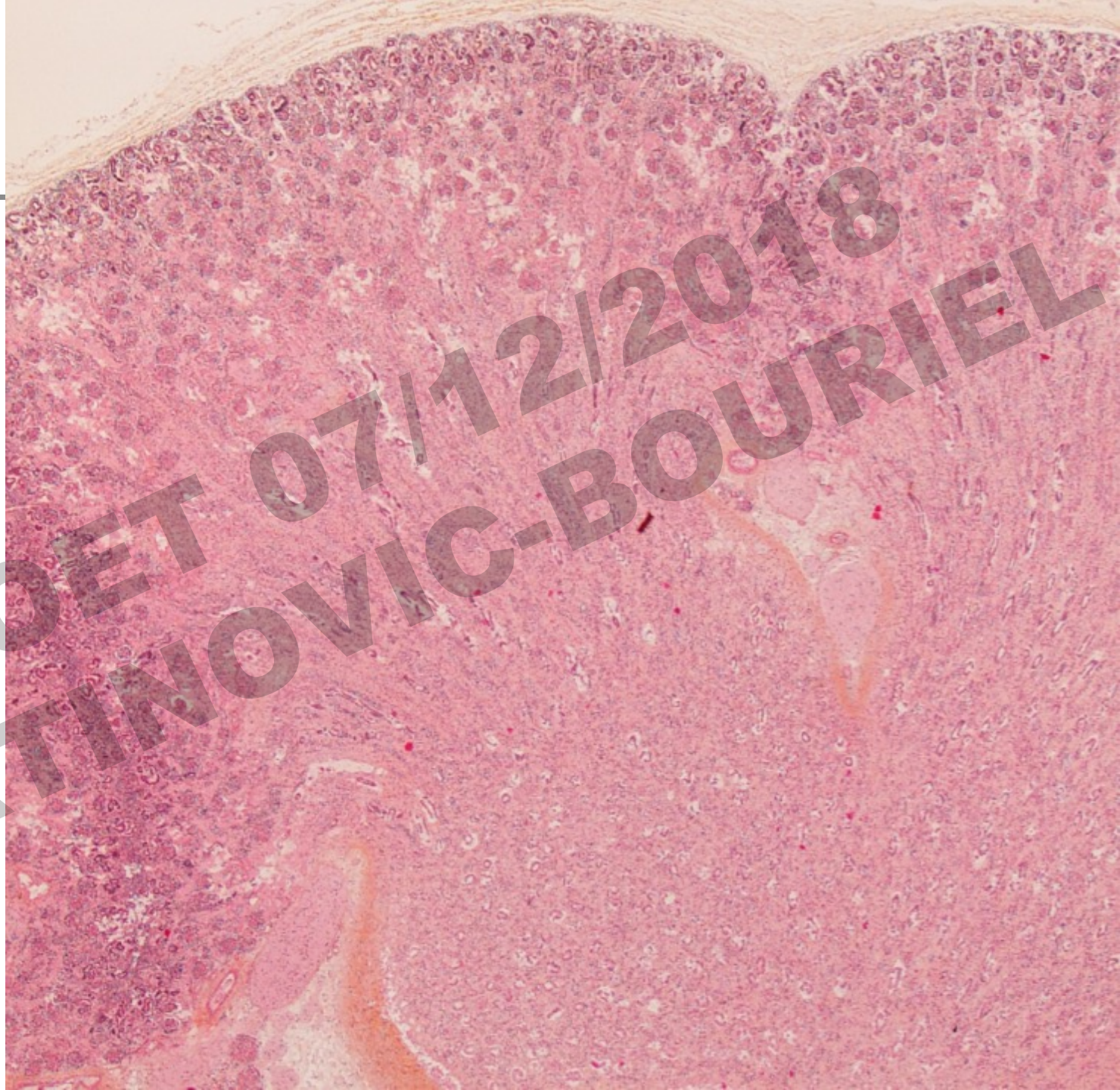
Individual hepatocyte  
LONB : 24-96h







4 layers of mature glomeruli:  
24w (96h)



SOFFOET 07/12/2018  
J. MARTINOVIC-BOURRIEL

## CASE 3

Fetal growth measurements : 24 weeks

Maceration = + 24h

X-ray discordance = IUGR

Bone maturation 24 w

Histology:

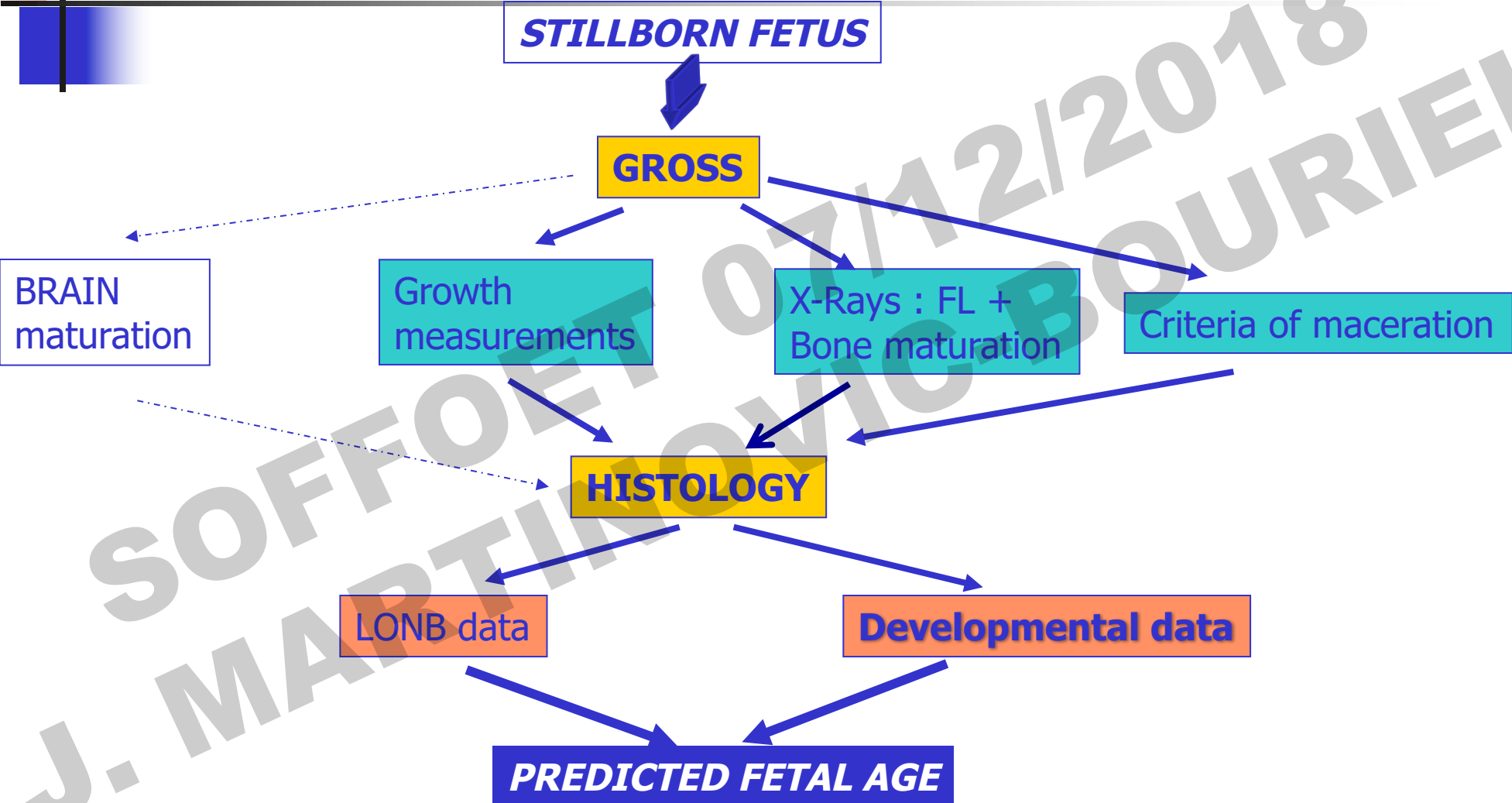
Renal maturation 24 w

Approx. 96h of retention





# SUMMERY : ALGORITHM





**THANK YOU**



Museum of Natural History, Paris