

ICG Fluorescence Imaging



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Background Fluorescence imaging of cancers

Clinical applications of fluorescence imaging to cancer surgery have been limited to:

- Malignant gliomas (five-aminolevulinic acid)¹
- Sentinel lymph nodes in breast cancers (Indocyanine green [ICG])²
- Liver cancers (ICG)^{3,4}

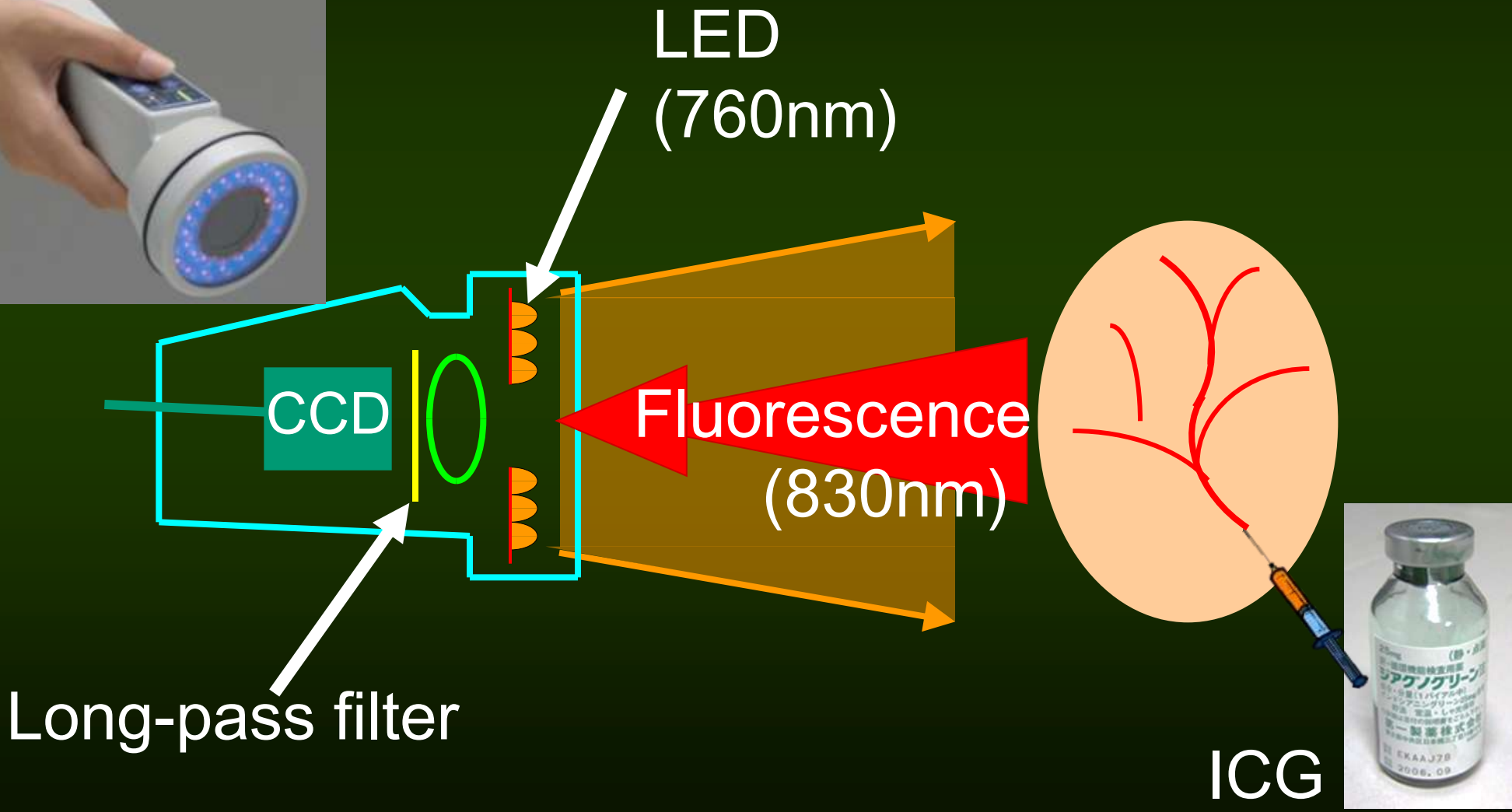
1. Stummer W. Neurosurgery 1998

2. Kitai T. Breast Cancer 2005

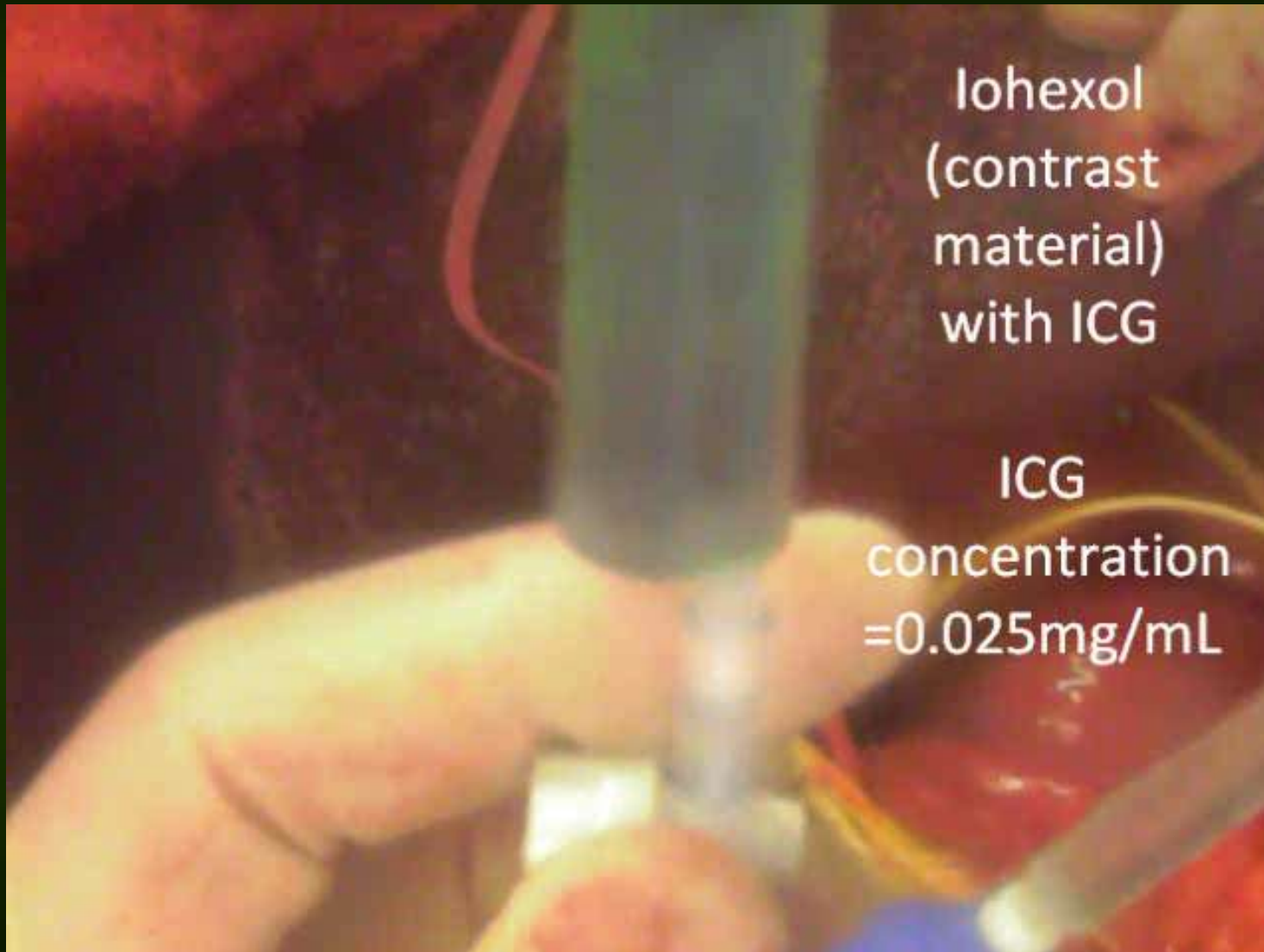
3. Ishizawa T & Kokudo N. Cancer 2009

4. Gotoh K. J Surg Oncol 2009

Background ICG-fluorescence imaging

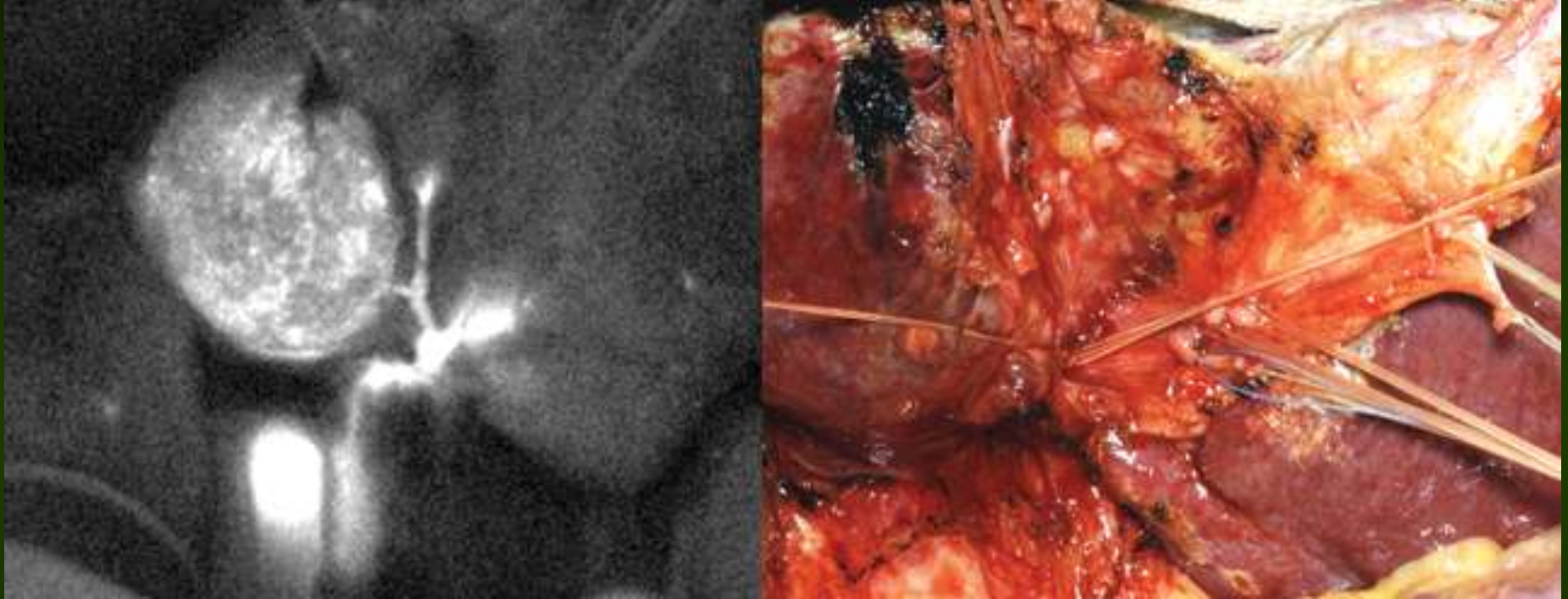


Background ICG-fluorescent cholangiography

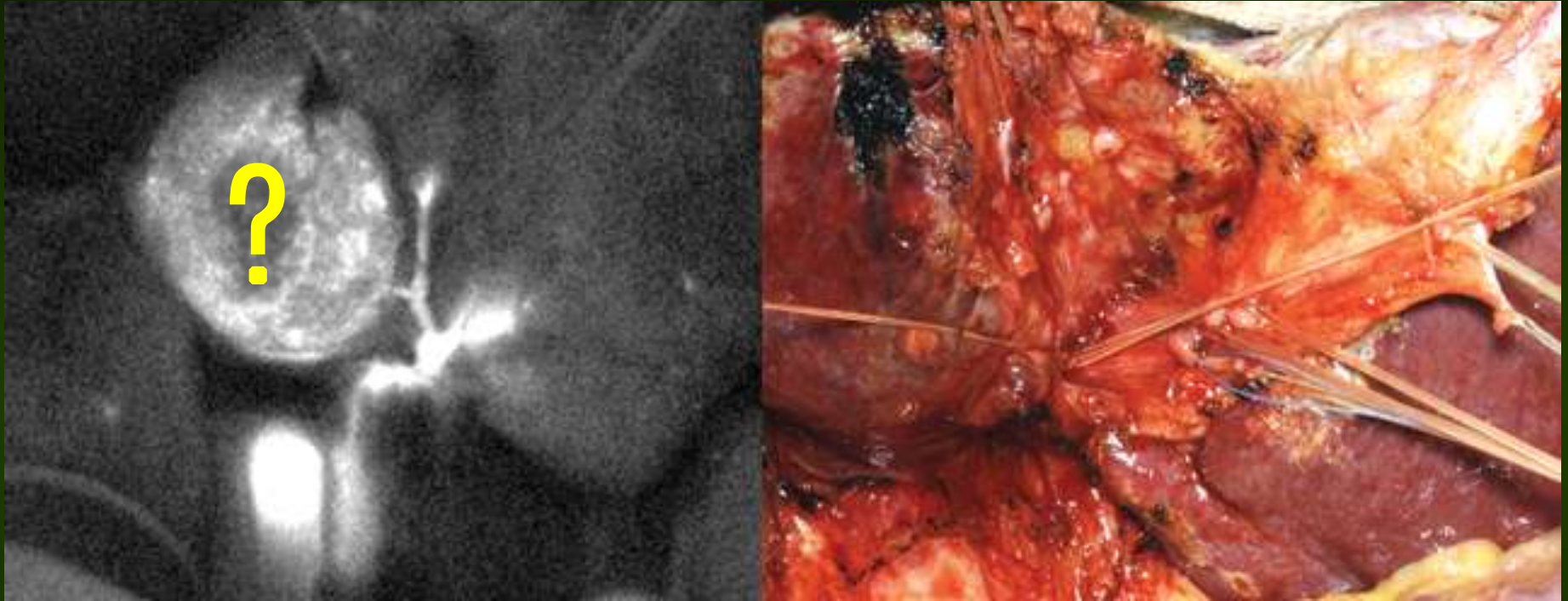


Kawaguchi, Ishizawa, Kokudo. JACS 2011

Background ICG-fluorescent cholangiography

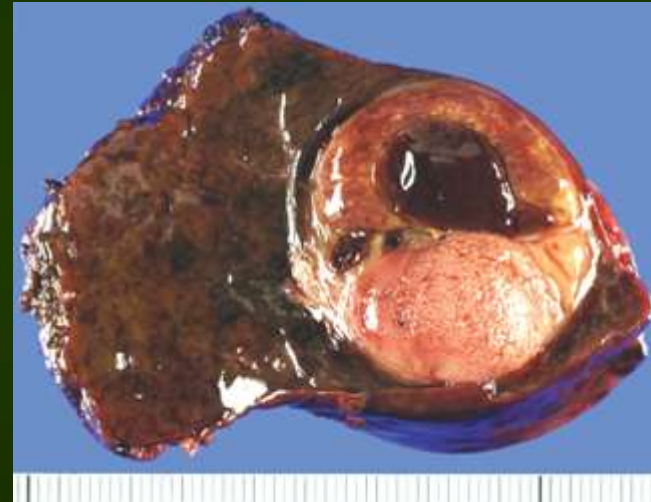


Background ICG-fluorescent cholangiography

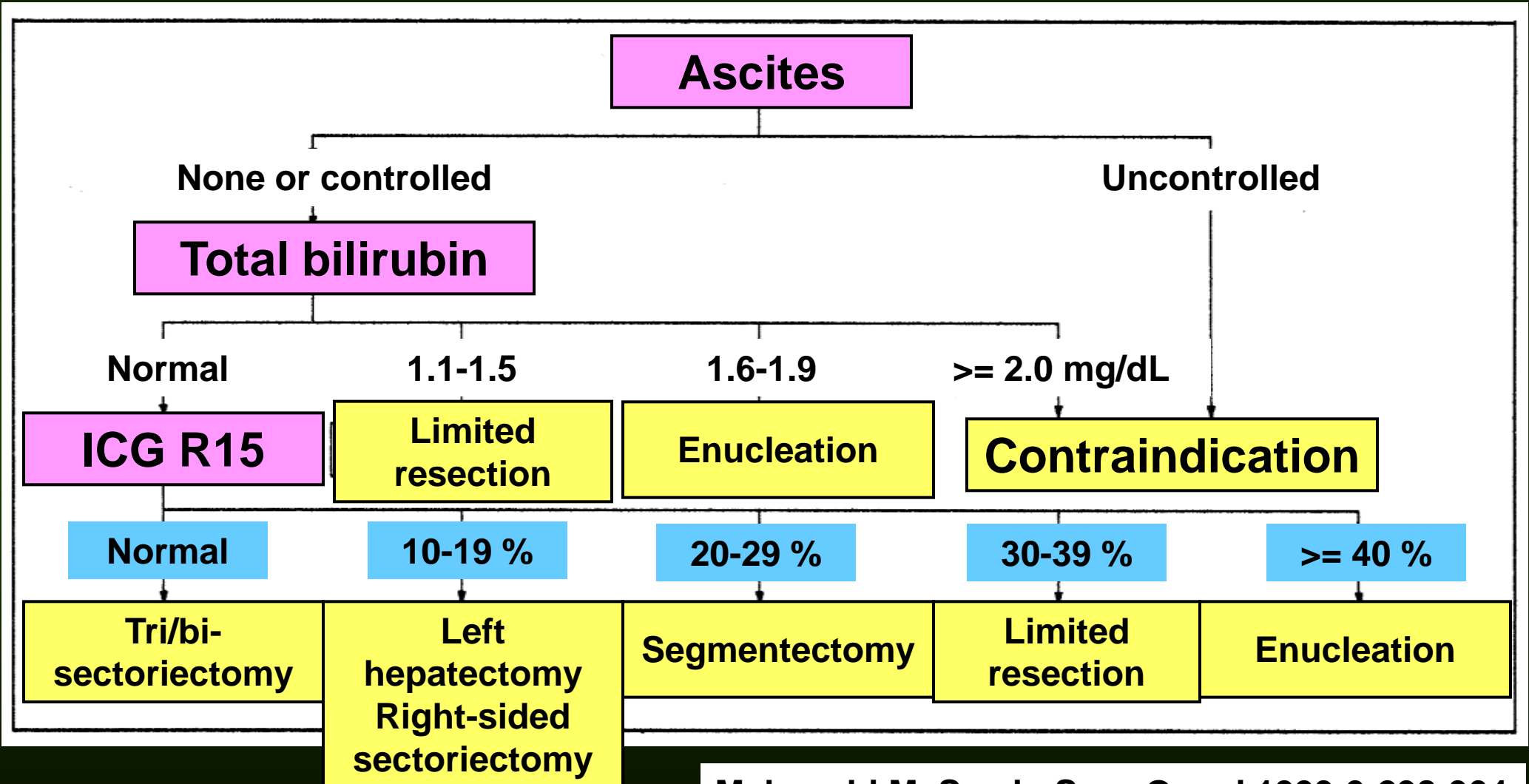


HCC shows fluorescence before ICG administration !!

Background Fluorescence imaging of HCC



Background Preoperative ICG-retention test



Background **Aims**

- 1) To demonstrate mechanistic background of ICG-fluorescent imaging of liver cancers
- 2) To introduce clinical applications of ICG-fluorescent imaging during liver resection

Methods of ICG-fluorescence imaging

Administration of ICG

- ICG (0.5 mg/kg) was intravenously injected within 2 weeks before surgery as part of a routine liver function test.

Methods of ICG-fluorescence imaging

Fluorescet imaging system

- 36 LEDs (760 nm) and a CCD camera, which can filter out light below 820 nm.



PDE (Hamamatsu Photonics, Hamamatsu, Japan)

Methods of ICG-fluorescence imaging

Examination on the liver surfaces

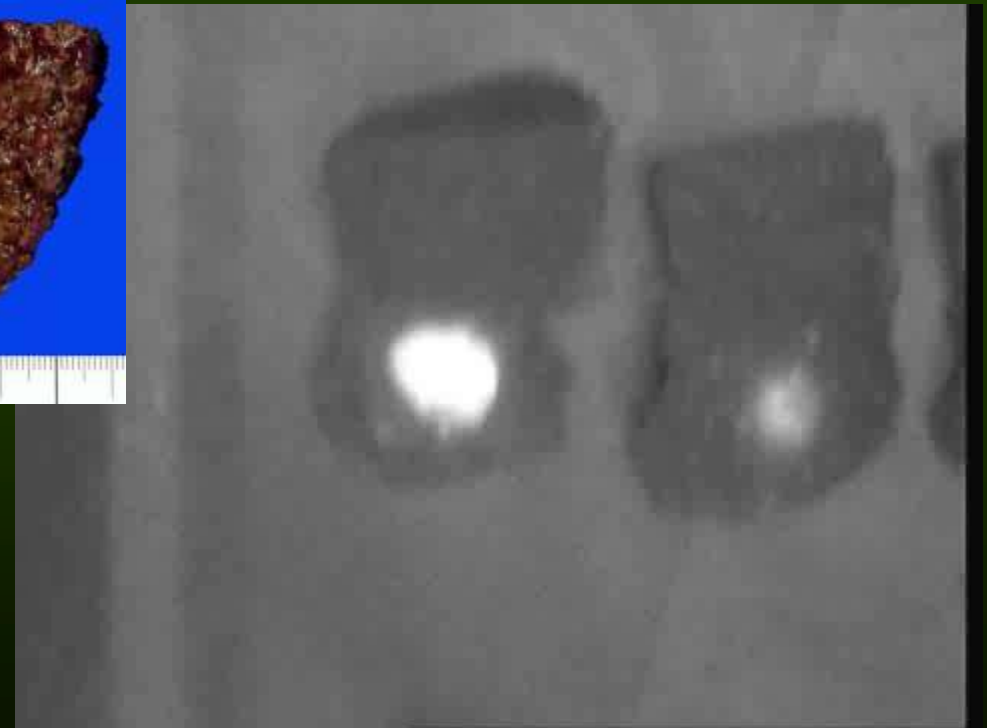
- Fluorescent images of liver surfaces were obtained using fluorescence imaging system.



Methods of ICG-fluorescence imaging

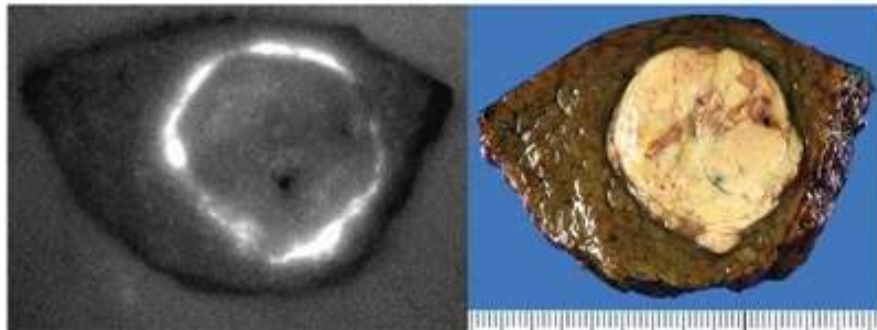
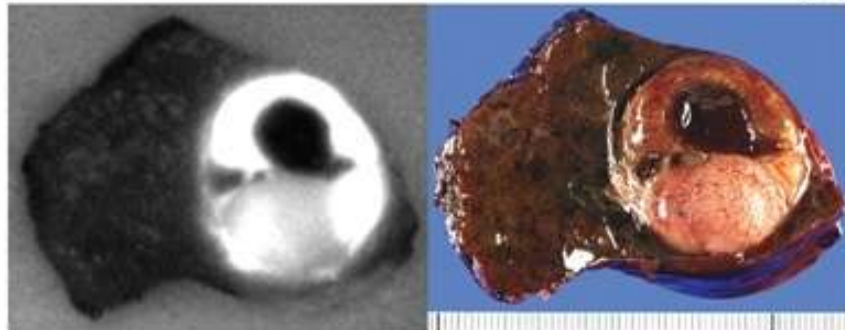
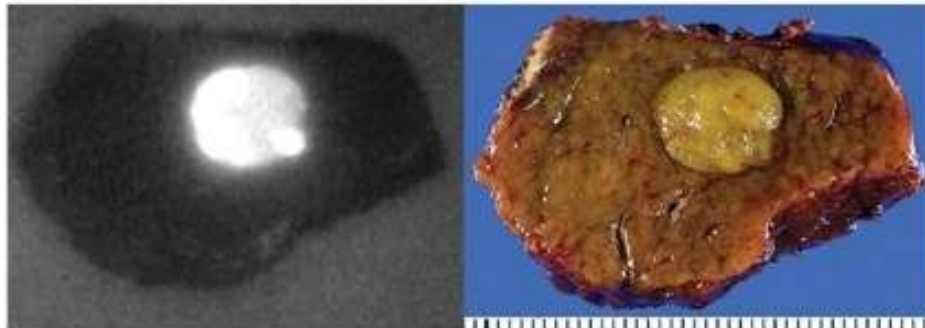
Examination on the resected specimens

- All of the cut surfaces were investigated following liver resection in the OR.



Fluorescent patterns of HCC

Differentiation n=277



Total	Well	58
	Moderate	72
	Poor	0

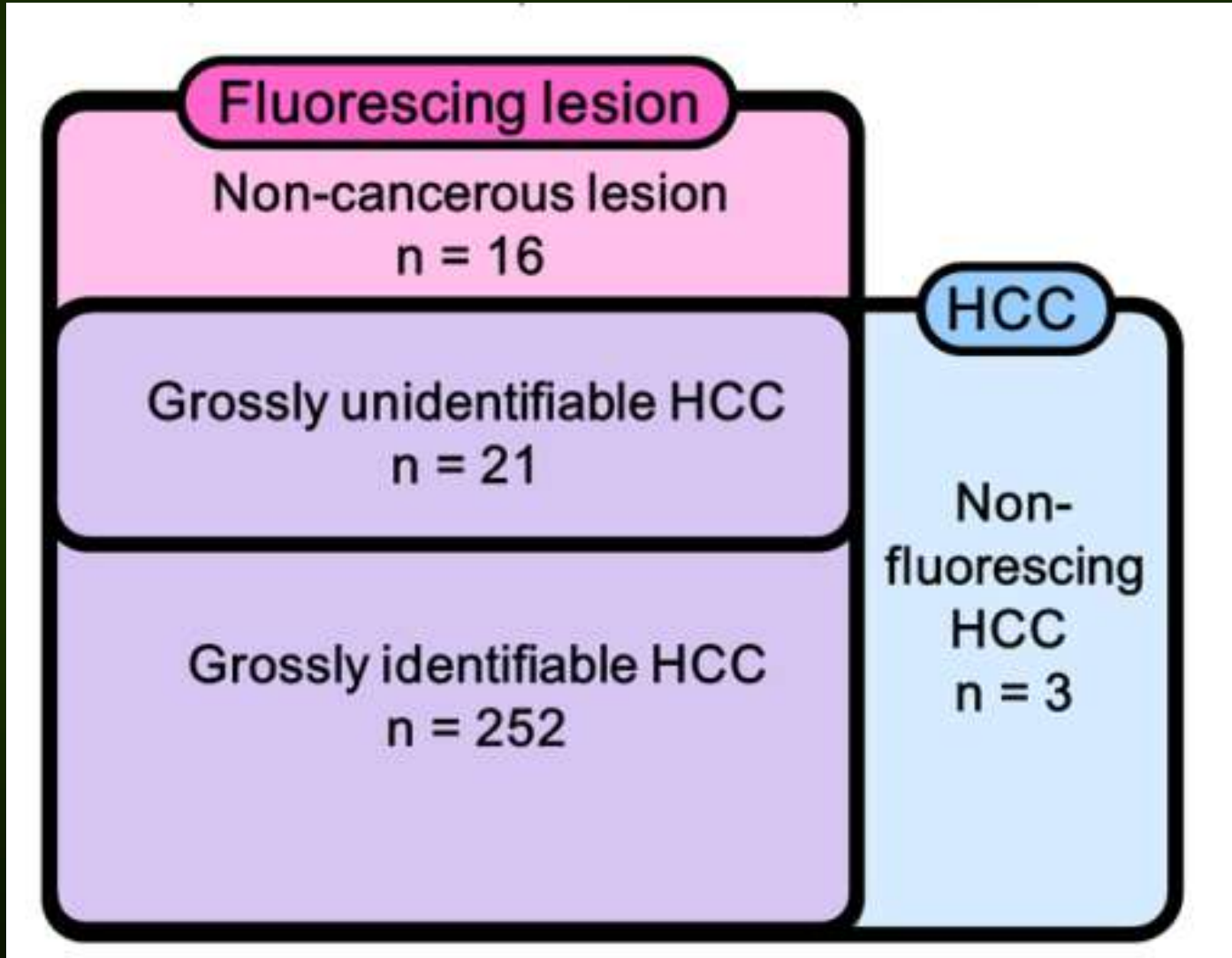
Partial	Well	9
	Moderate	100
	Poor	5

Rim	Well	1
	Moderate	14
	Poor	18

(Non-fluorescing HCCs, n = 3)

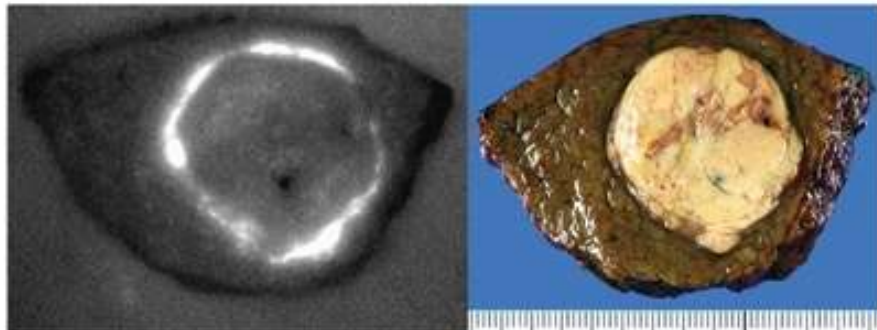
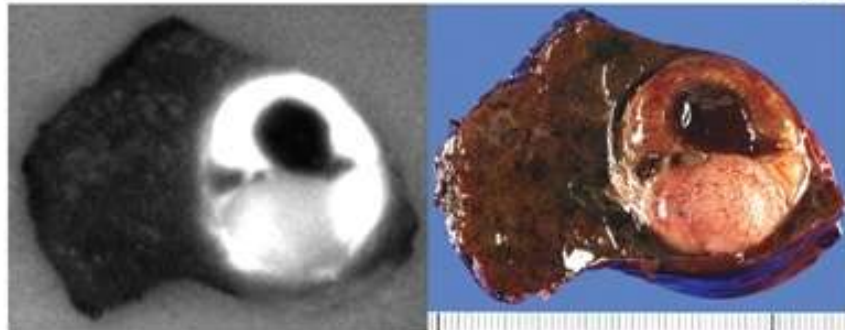
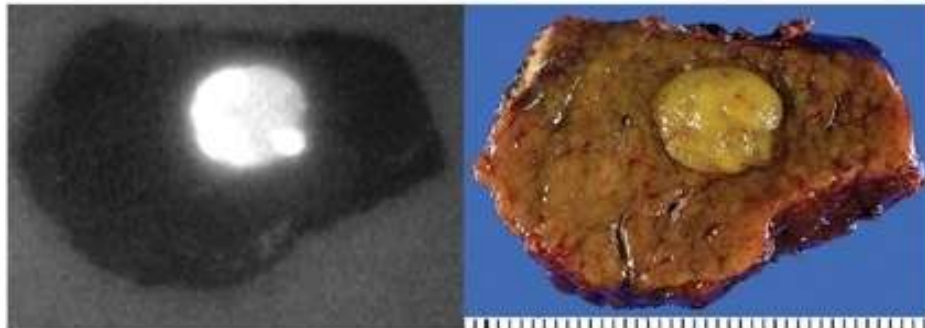
Cancer detectability of ICG-fluorescence imaging

- Sensitivity: 99%, PPV: 94%



Fluorescent patterns of HCC

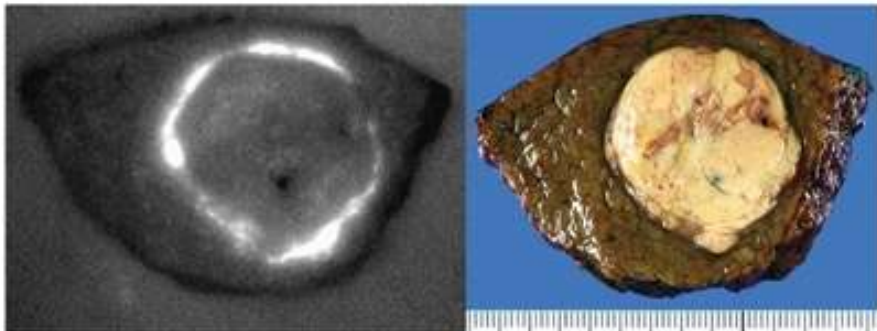
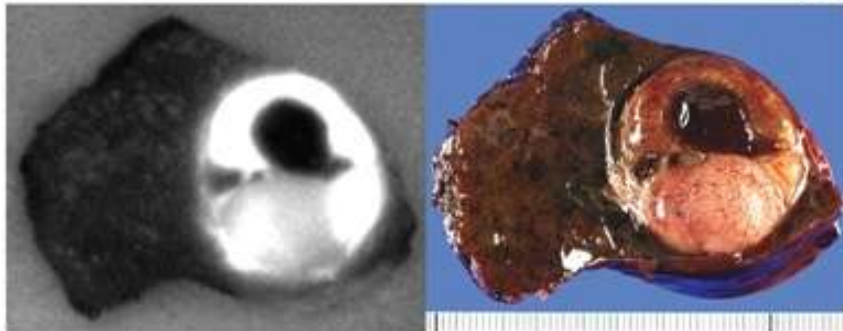
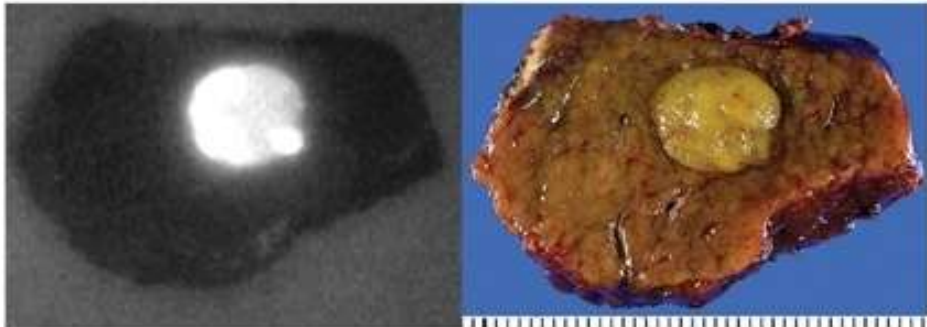
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(Non-fluorescing HCCs, n = 3)

Fluorescent patterns



Total

Partial

Cancerous
fluorescence
(c)

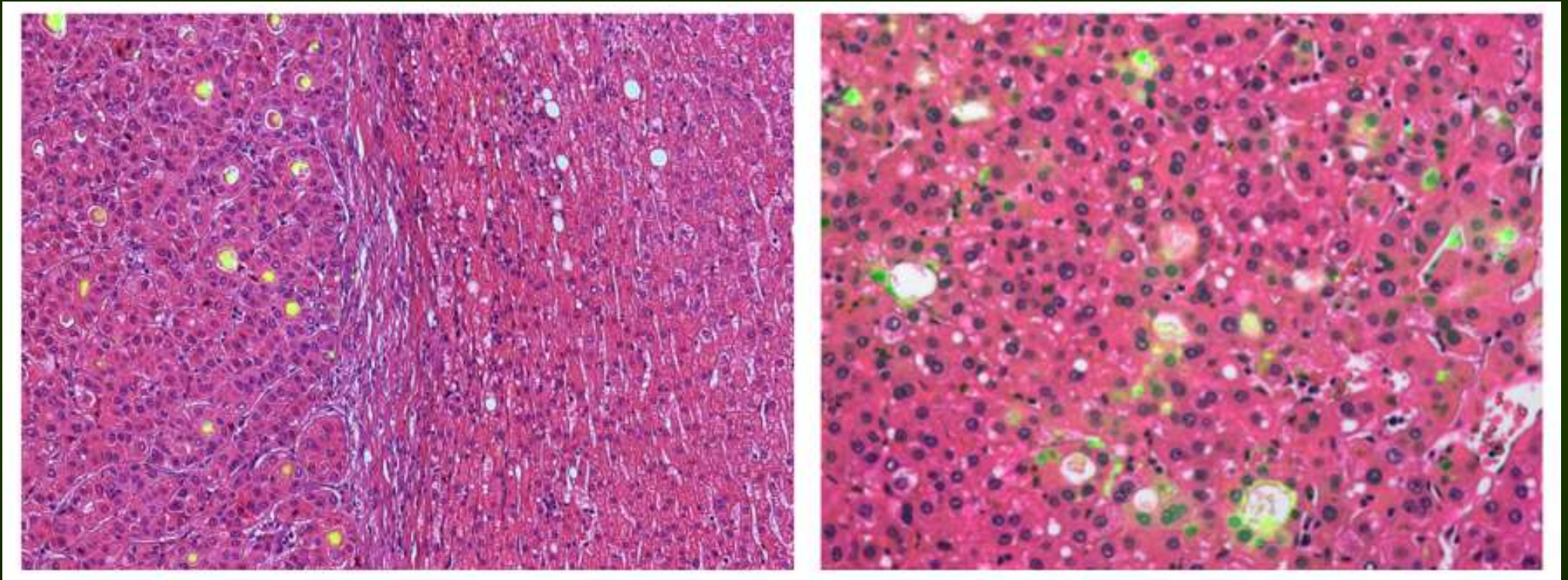
Rim



(r)

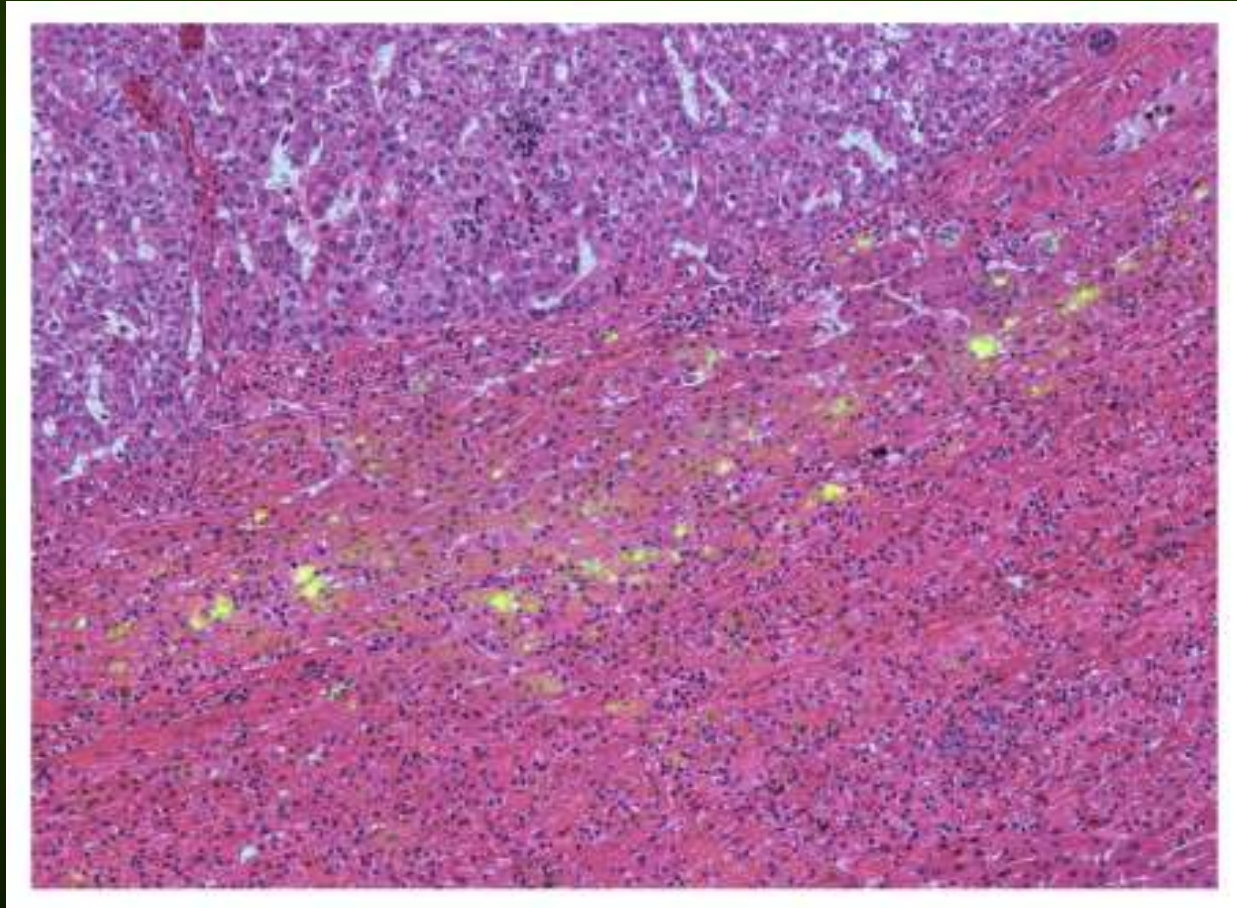
Fluorescent microscopy

HCC showing cancerous fluorescence



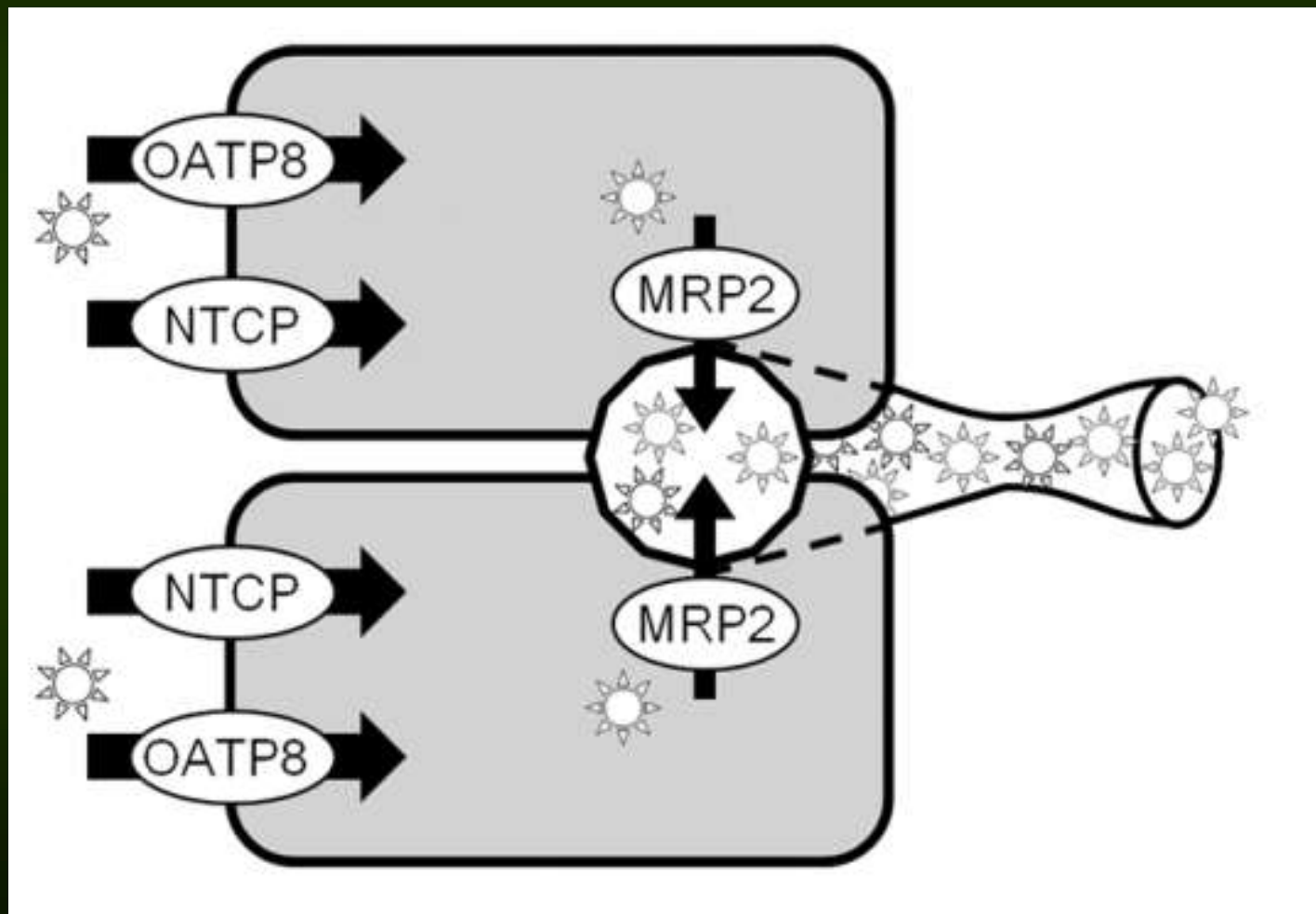
Fluorescent microscopy

HCC showing rim-type fluorescence

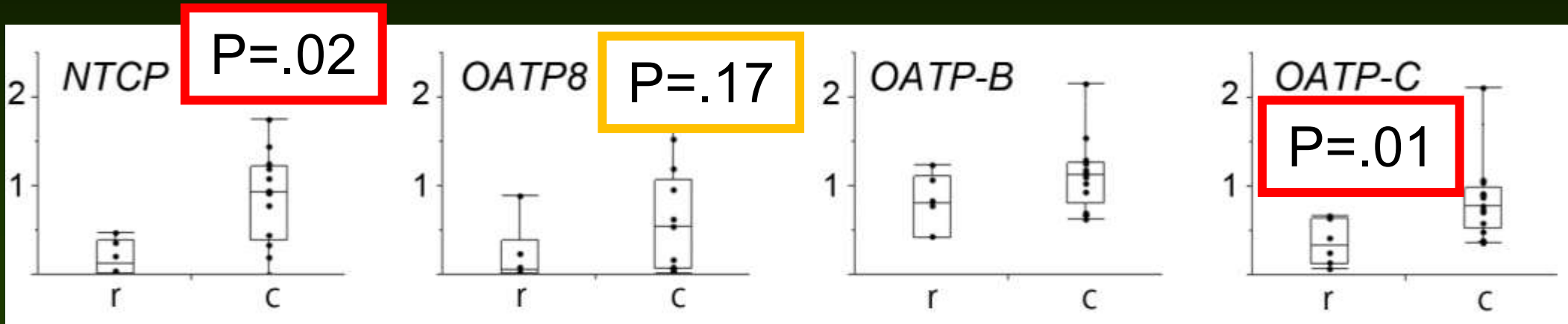


Mechanistic background of ICG-fluorescence imaging of HCC

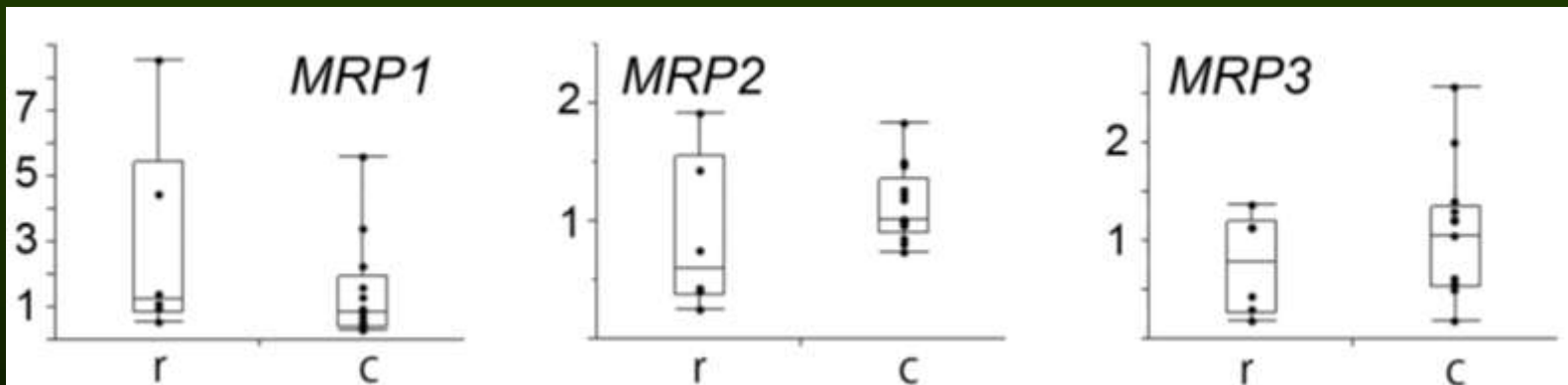
Non-cancerous liver



C/N ratio of gene expression (n = 19)



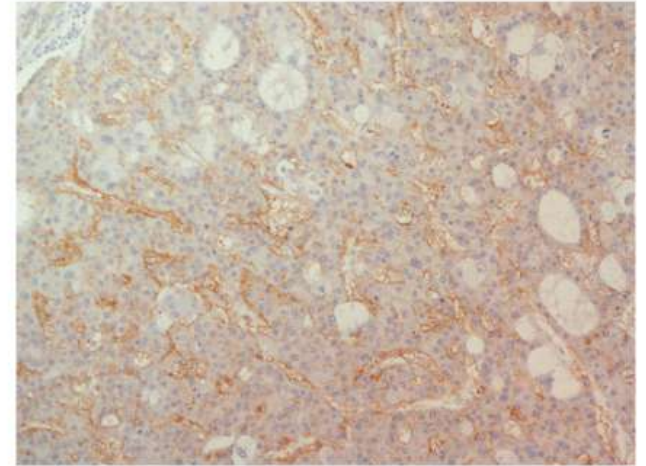
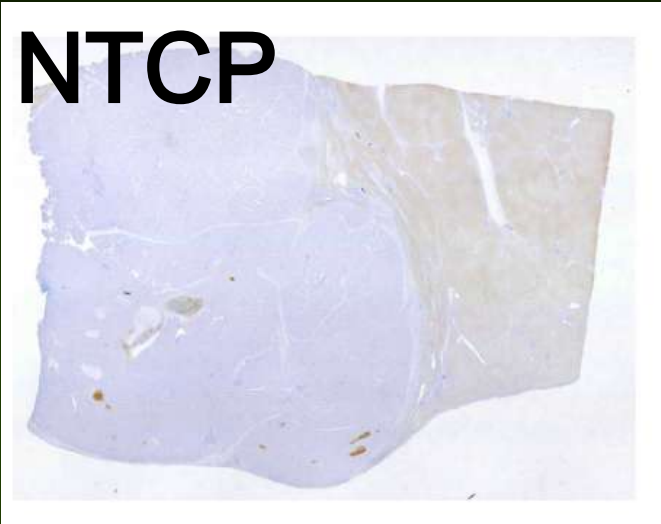
Uptake transporters



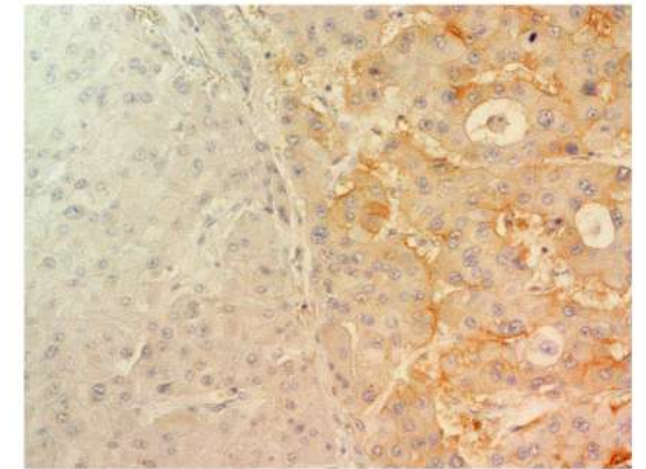
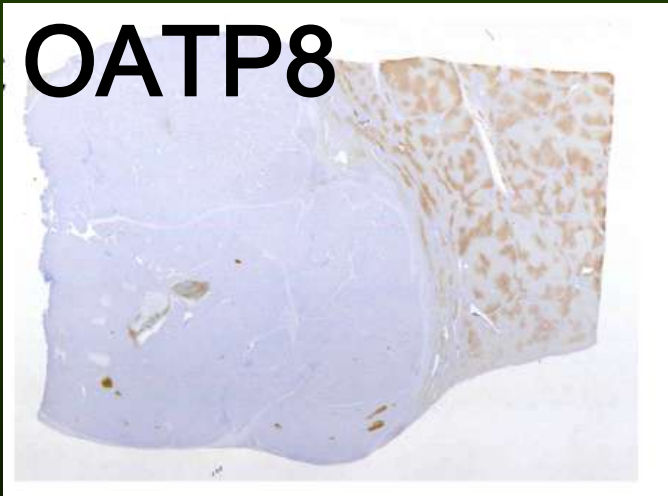
Excretion transporters

Immunohistochemical staining

NTCP



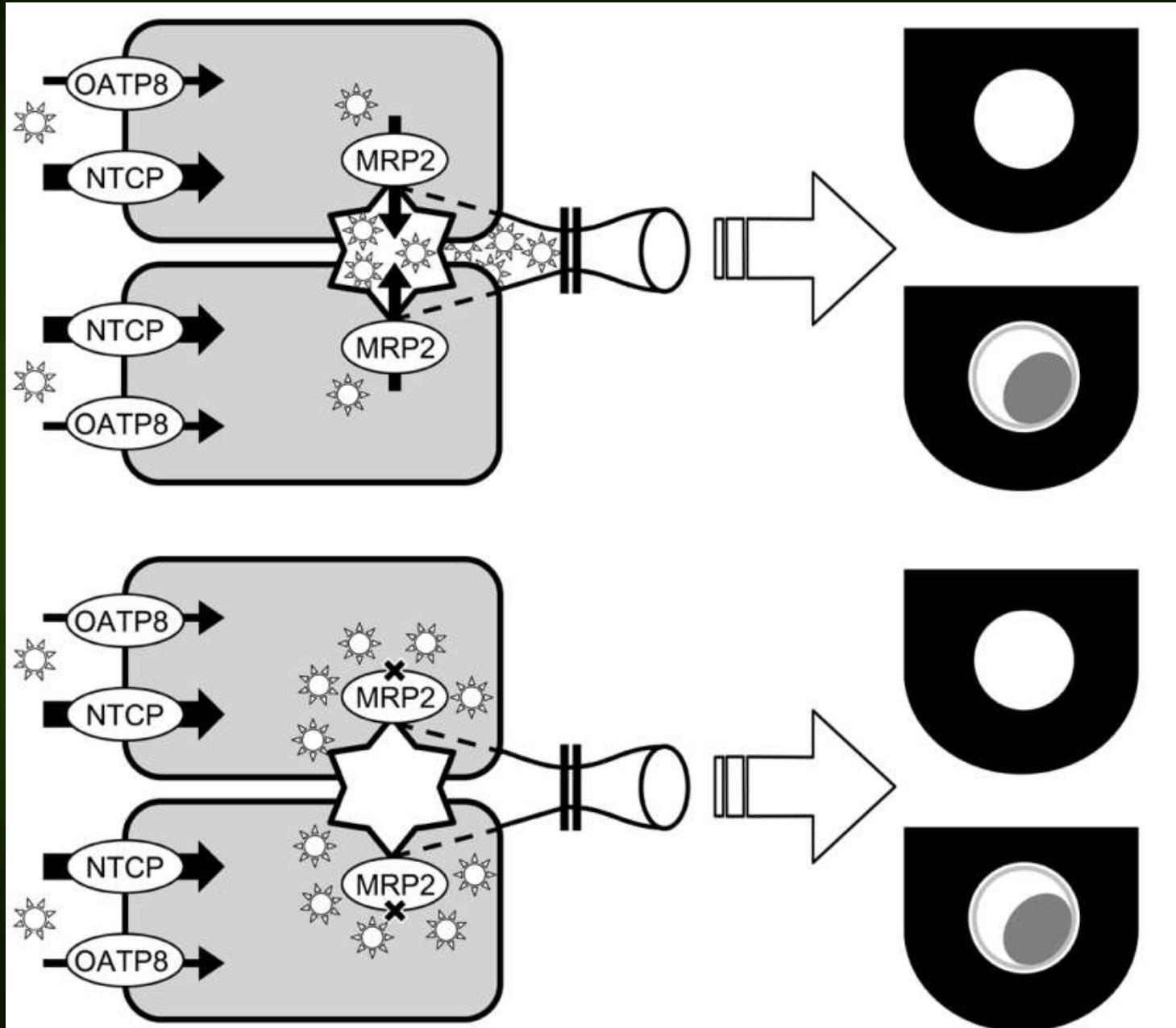
OATP8



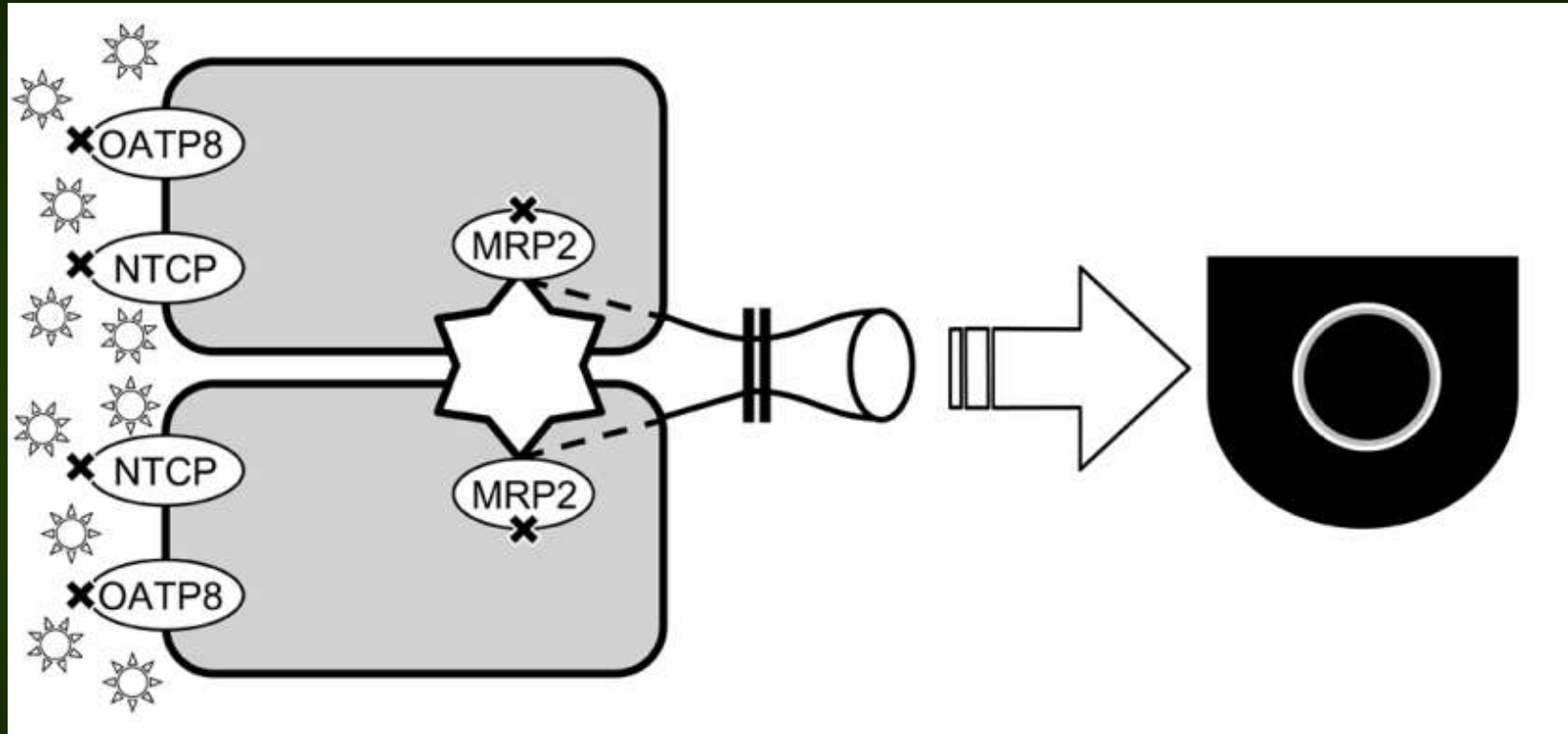
Rim-type

Cancerous-type

Cancerous-type HCC

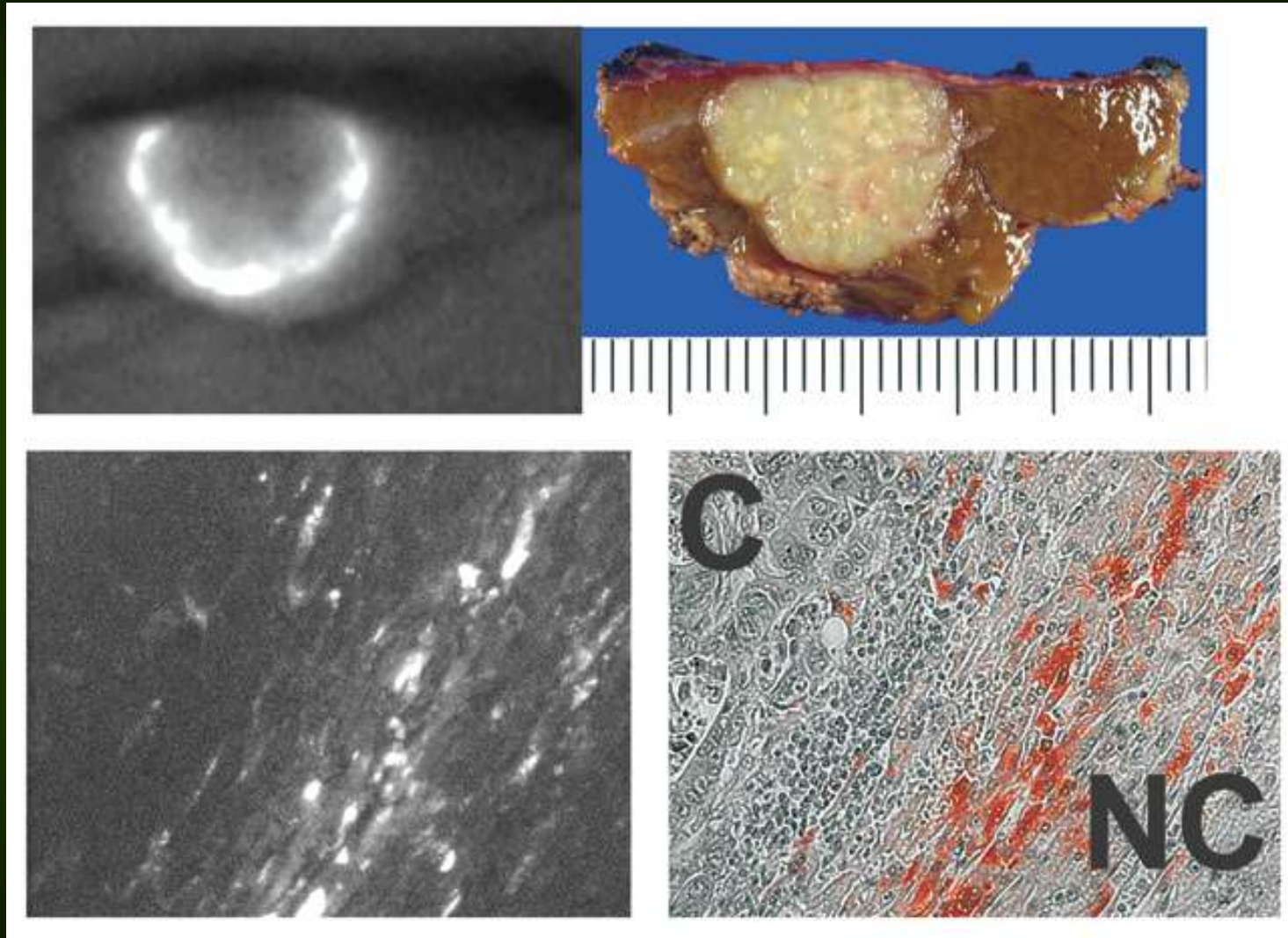


Rim-type HCC

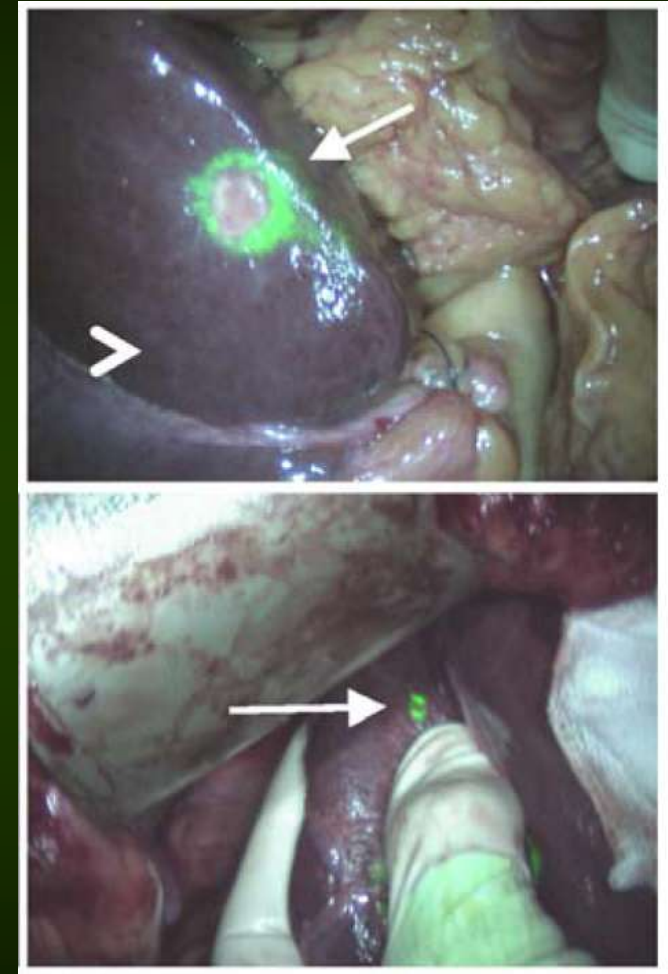
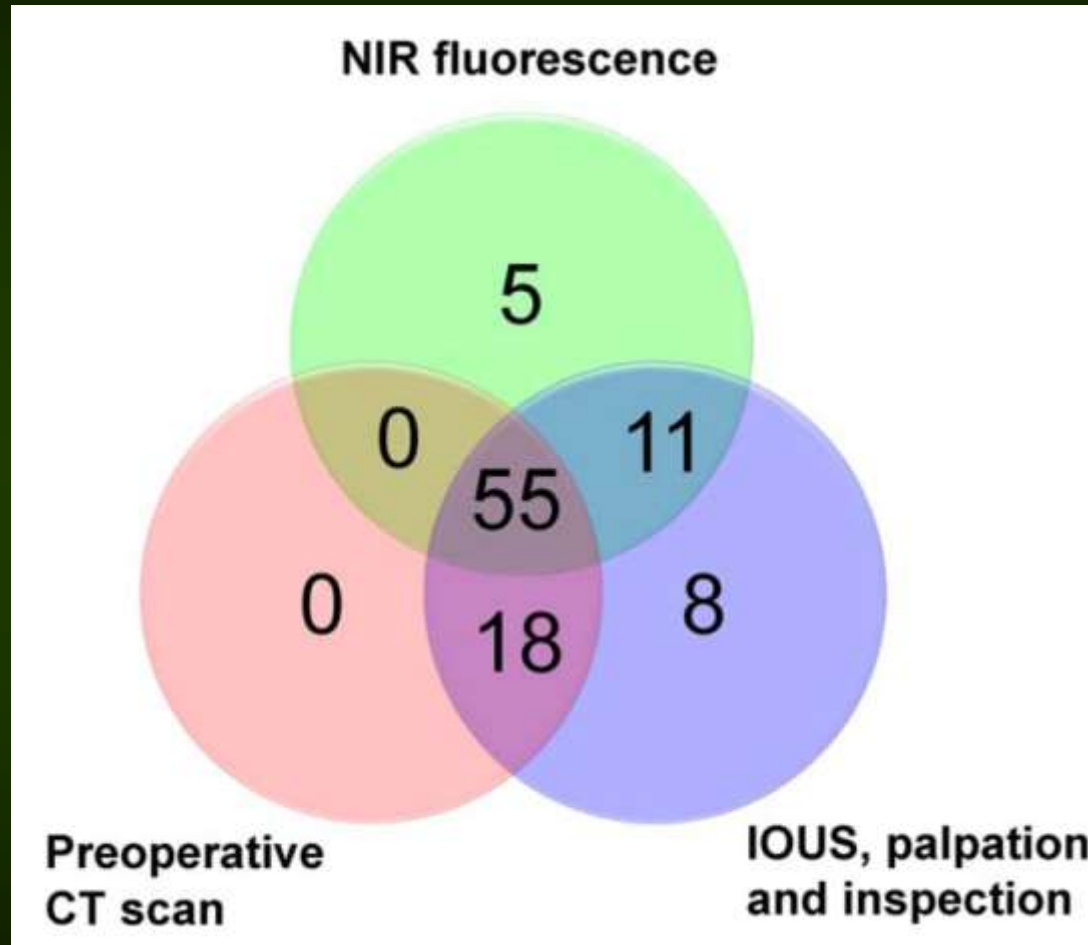


Ishizawa and Kokudo. Ann Surg Oncol 2013

ICG-fluorescence imaging of CRLM

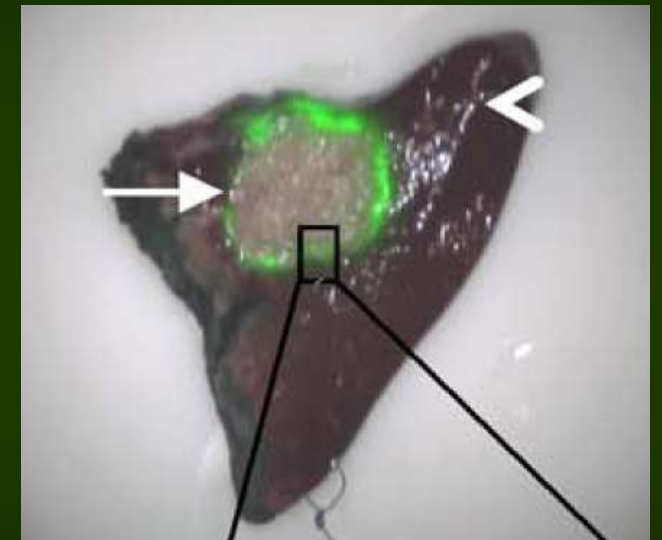
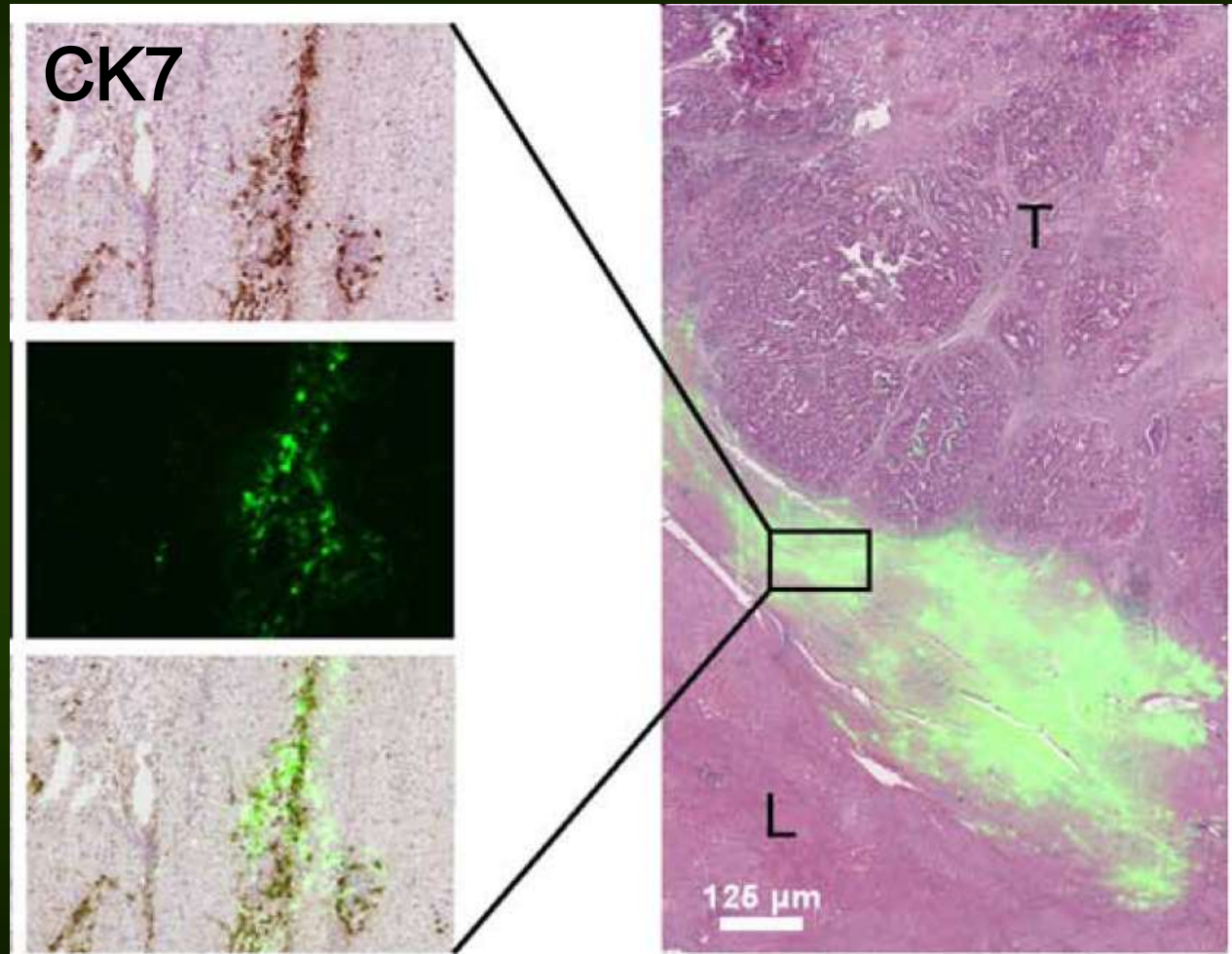


ICG-fluorescence imaging of CRLM



van der Vorst JR, Frangioni JV, Vahrmeijer AL. Cancer 2013

ICG-fluorescence imaging of CRLM



van der Vorst JR, Frangioni JV, Vahrmeijer AL. Cancer 2013

Clinical application of ICG-fluorescence imaging

Advantages:

- Safety and feasibility
- High sensitivity
- Real-time examination

Limitations:

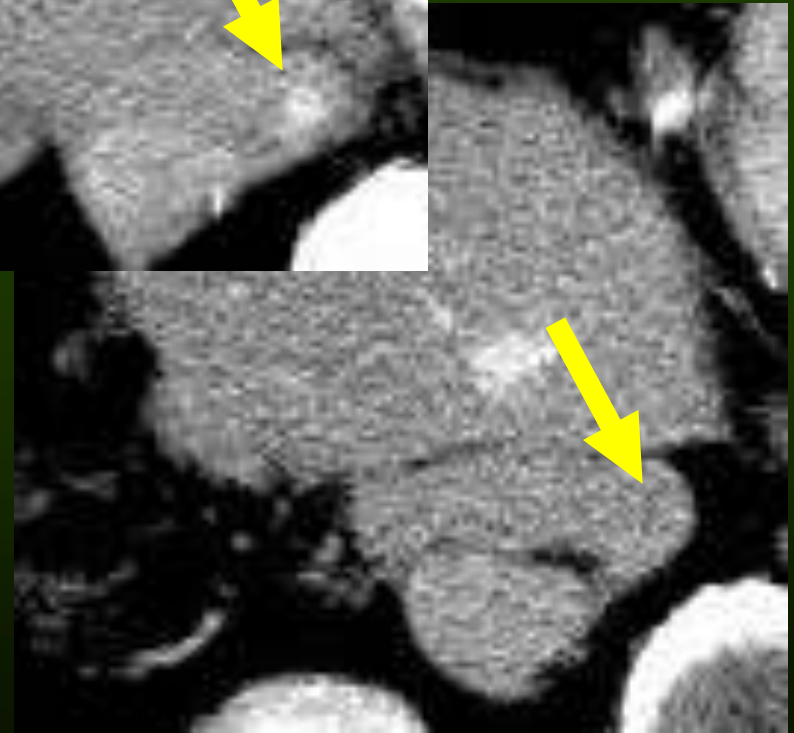
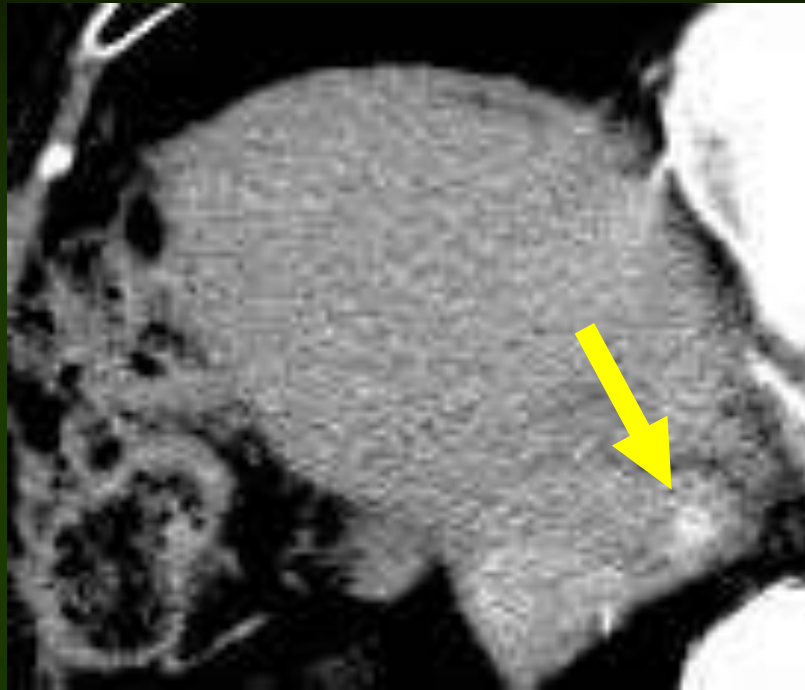
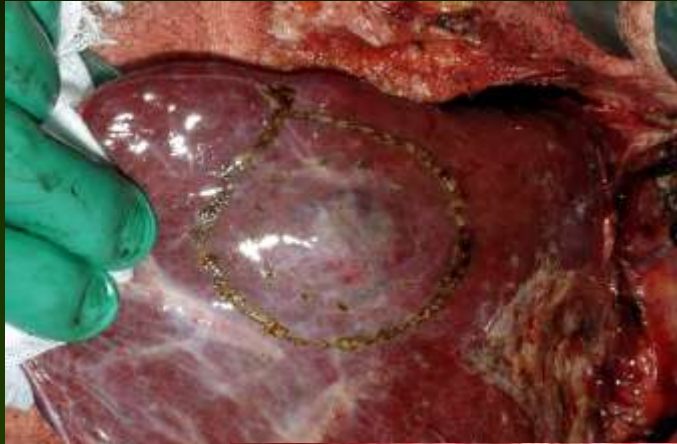
- Tissue permeability (up to 5-10 mm)
- False positives

Clinical application of ICG-fluorescence imaging

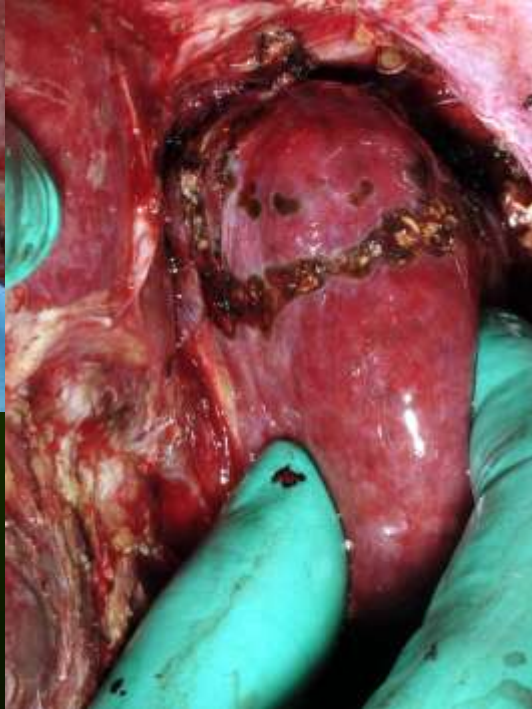
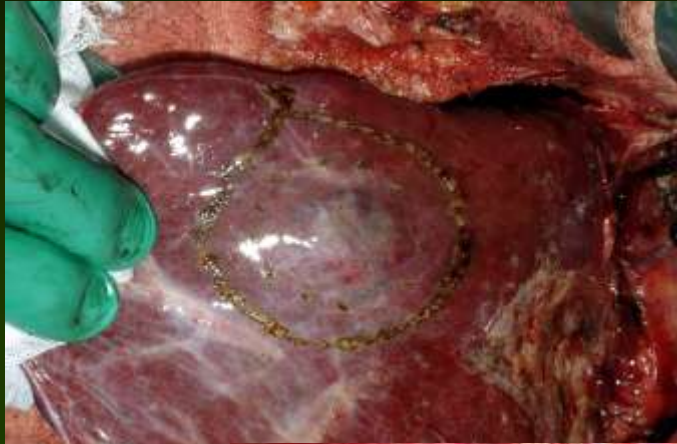
Expected role of ICG-fluorescent imaging is to detect.....

- peripherally-located but invisible liver cancer
- new lesions to be resected (close to ϕ 1cm)
- HCC tissues left on the raw surface
- small (early) HCCs in the resected specimen
- cholestatic areas caused by cancer invasion

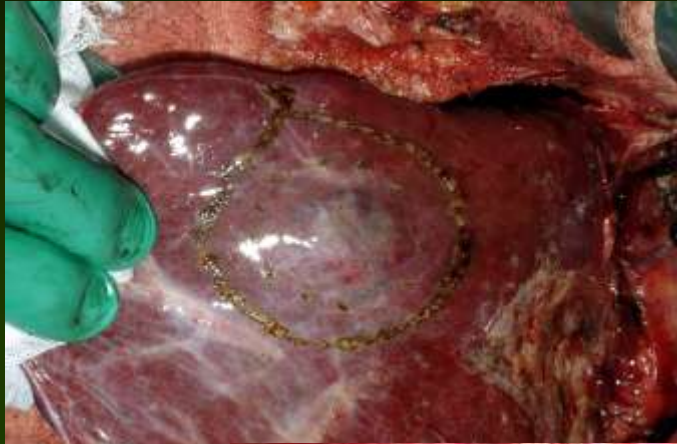
Case 1 Identification of HCC before resection



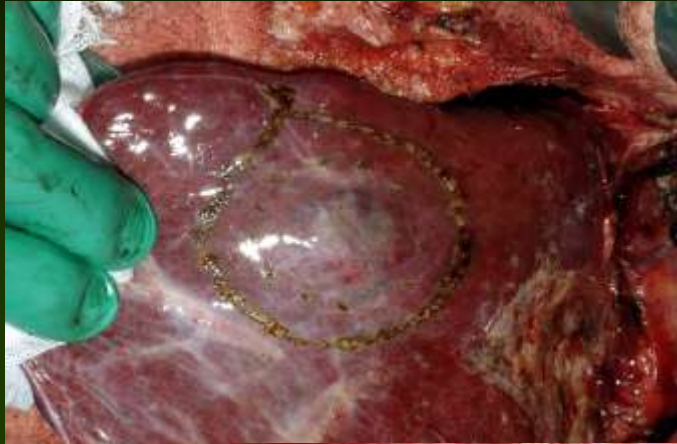
Case 1 Identification of HCC before resection



Case 1 Identification of HCC before resection



Case 1 Identification of HCC before resection



Case 2 Identification of HCC (laparoscope)

Laparoscopic partial hepatectomy (S VI)
using ICG-fluorescence imaging

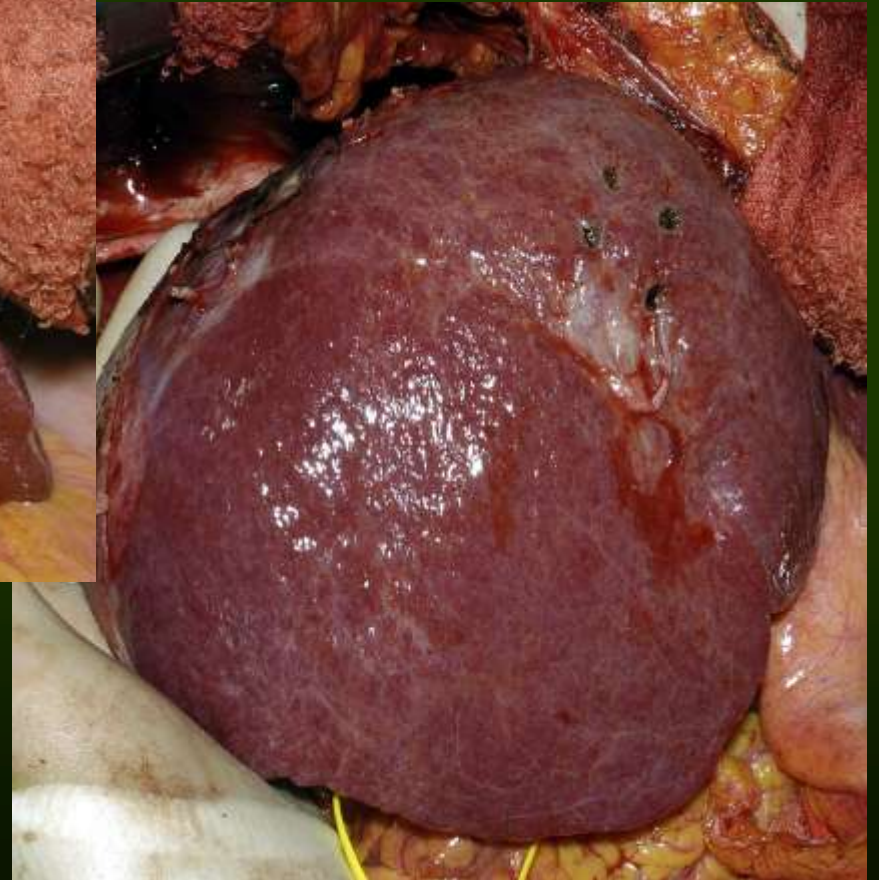
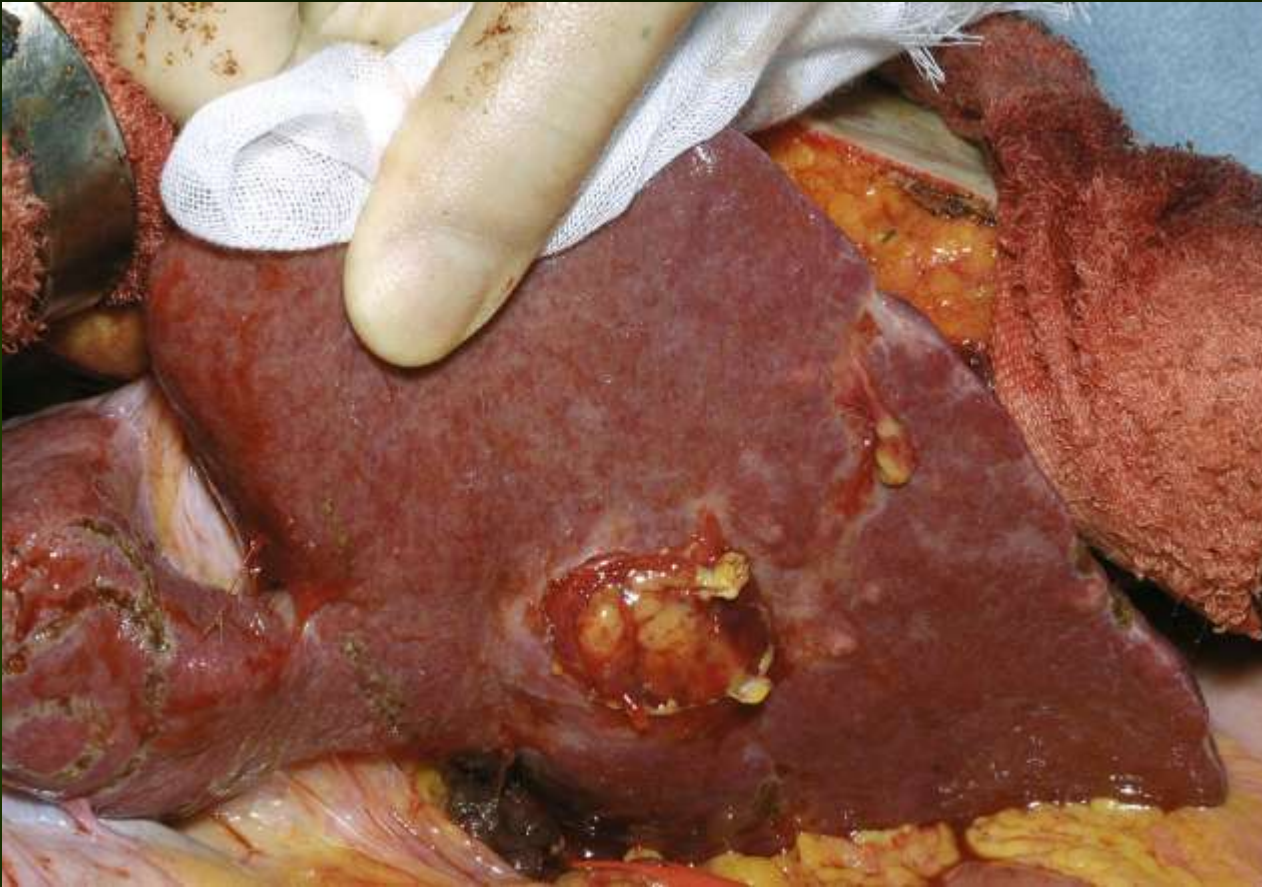
University of Tokyo
Ishizawa T, Kokudo N

Clinical application of ICG-fluorescent imaging

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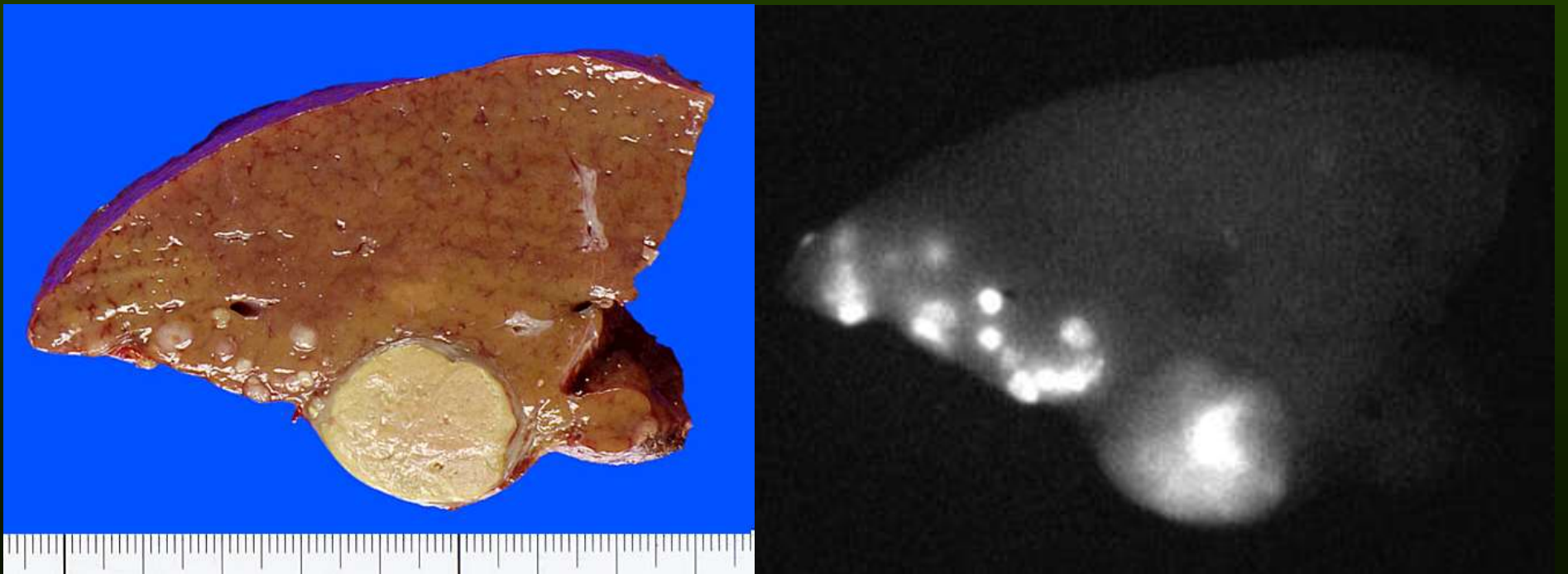
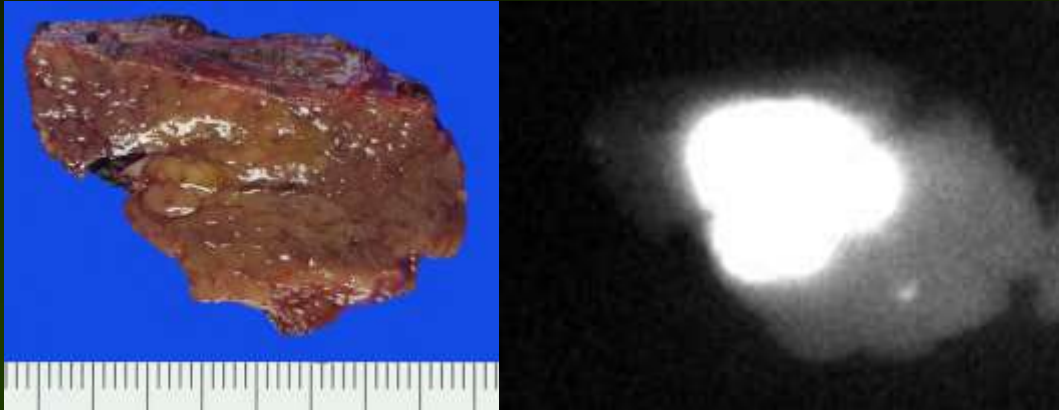
Case 3 Identification of HCC before resection



Case 3 Identification of HCC before resection



Case 3 Identification of HCC before resection

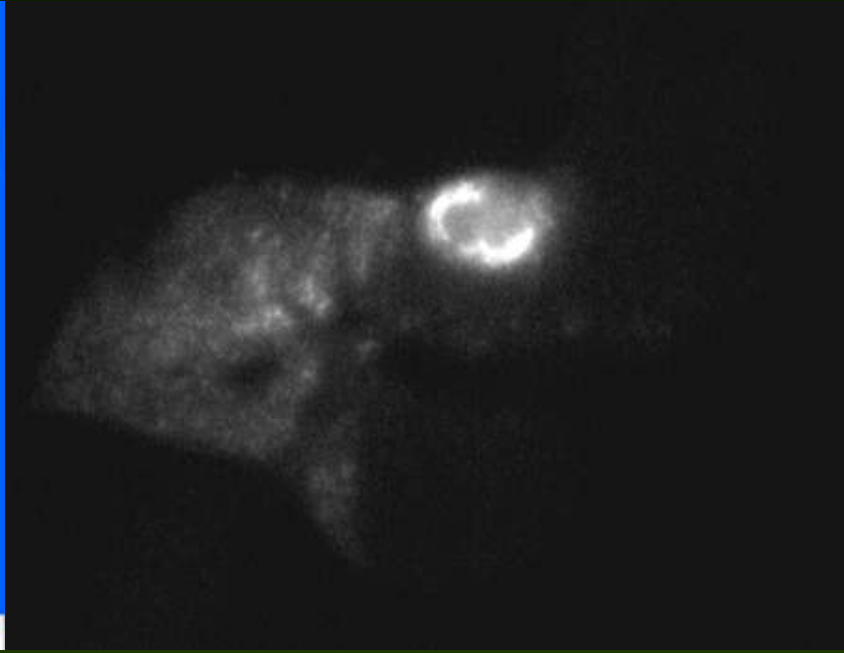


Clinical application of ICG-fluorescent imaging

Expected role of ICG-fluorescent imaging is to detect.....

- peripherally-located but invisible liver cancer
- new lesions to be resected (close to ϕ 1cm)
- **HCC tissues left on the raw surface**
- small (early) HCCs in the resected specimen
- cholestatic areas caused by cancer invasion

Case 4 Examination of the raw surface



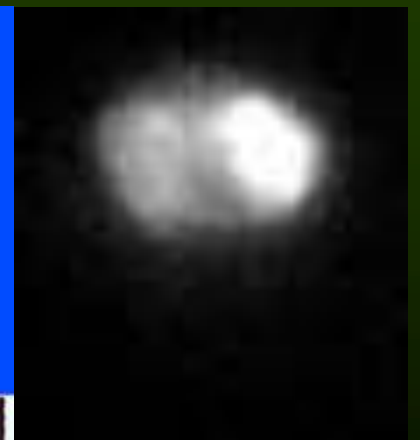
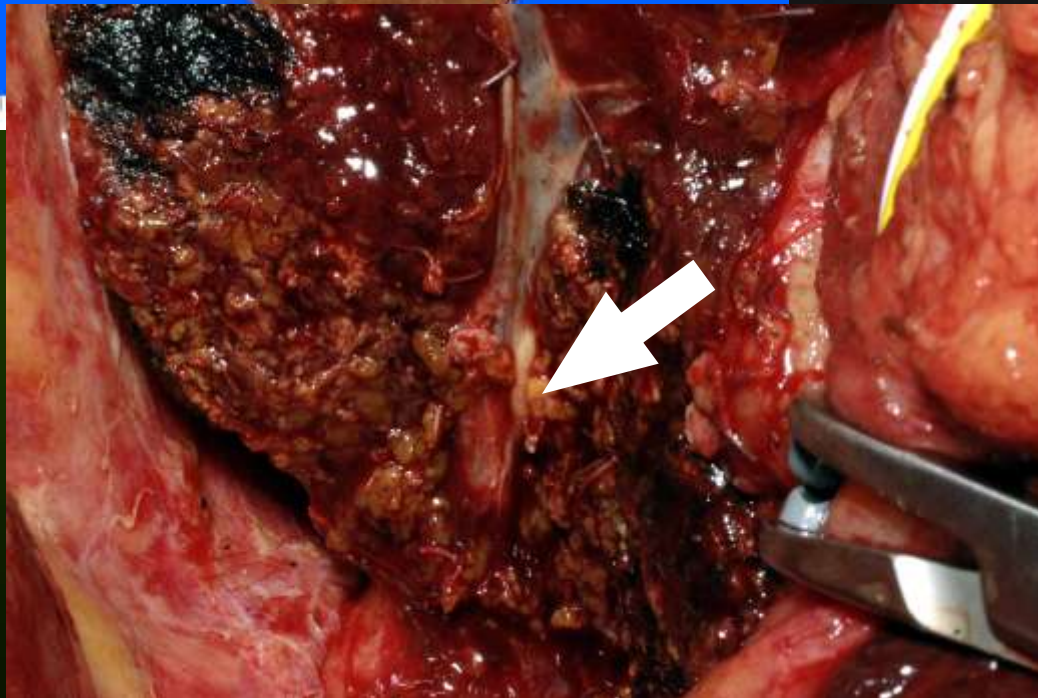
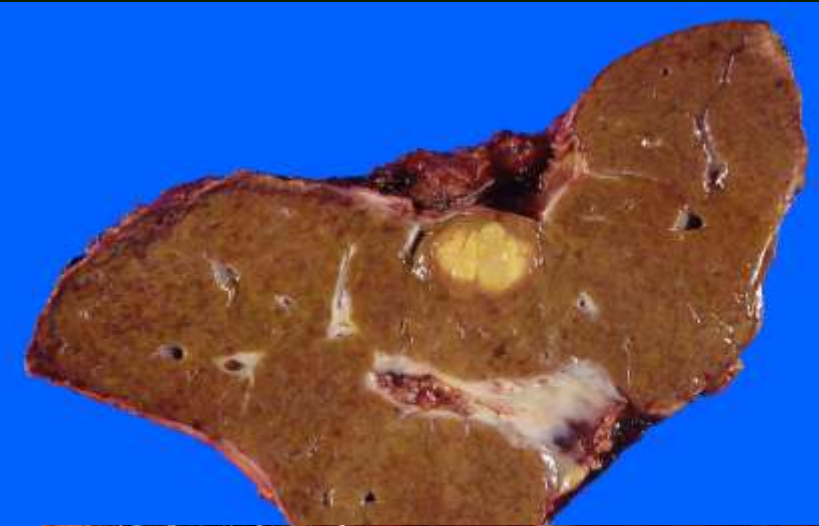
Case 4 Examination of the raw surface



Fluorescent lesions on the raw surface of the liver after resection

The image shows a dark, textured surface, likely the raw surface of a liver after resection. A bright, glowing spot is visible in the center, indicating a fluorescent lesion. The background is dark and grainy, with some faint, curved lines suggesting the shape of the organ.

Case 4 Examination of the raw surface

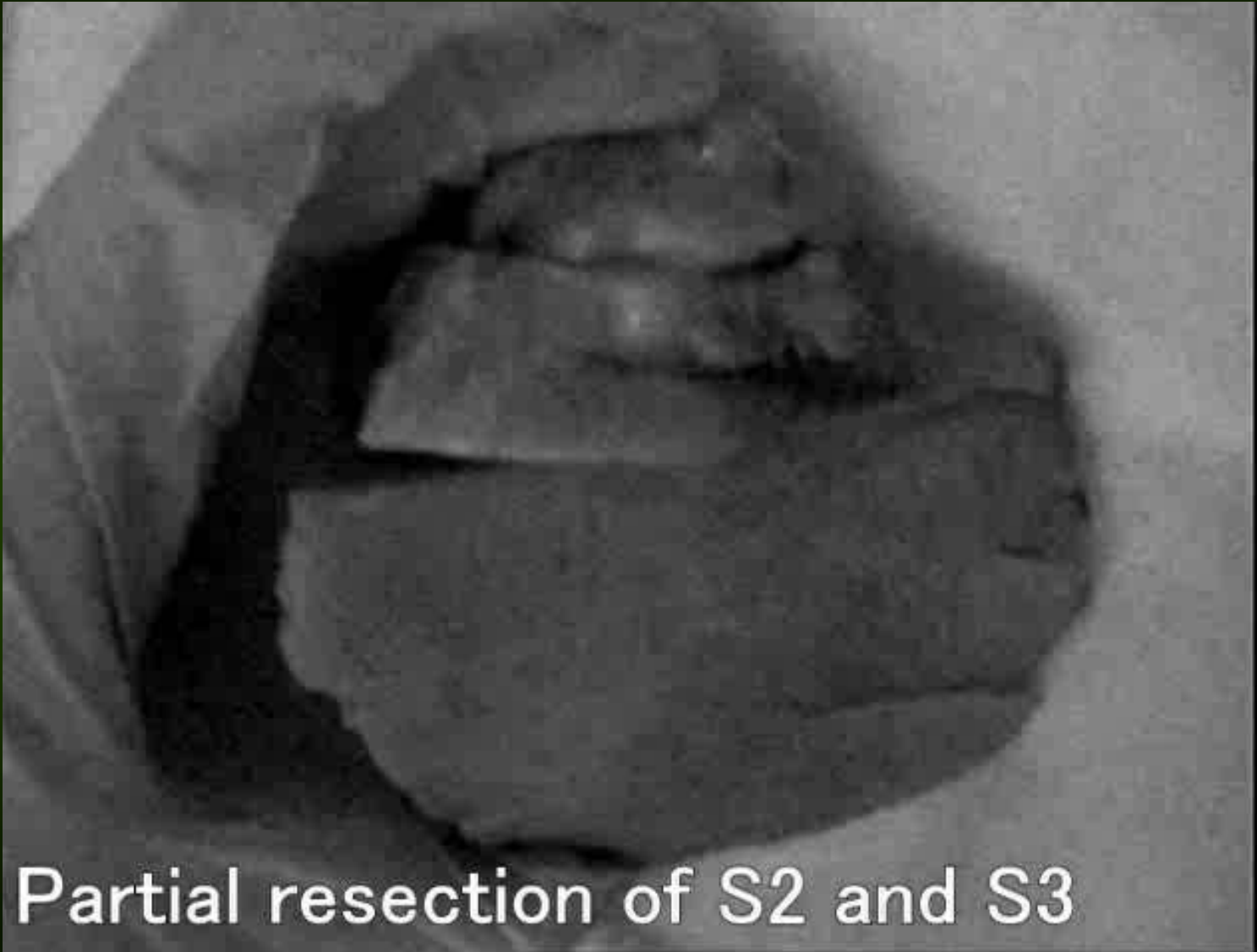


Clinical application of ICG-fluorescent imaging

Expected role of ICG-fluorescent imaging is to detect.....

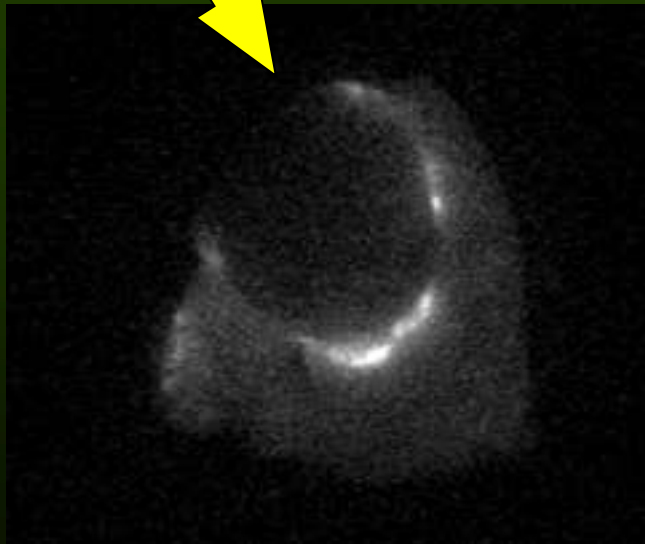
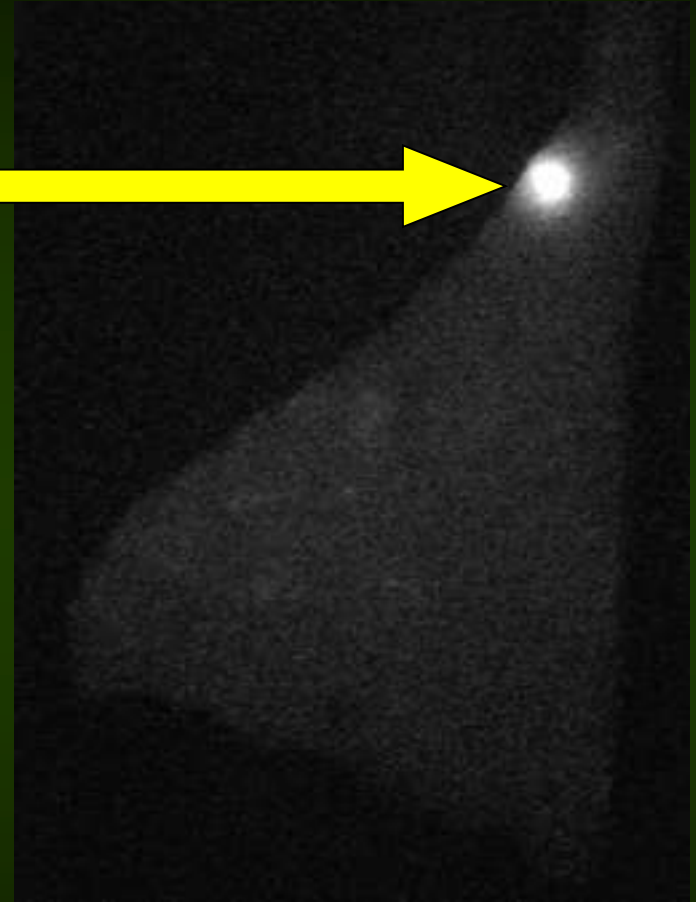
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Case 5 Examination of the resected specimen

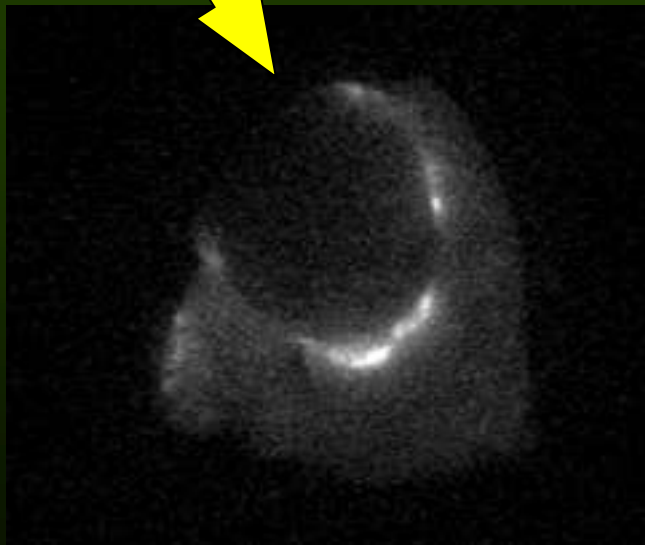
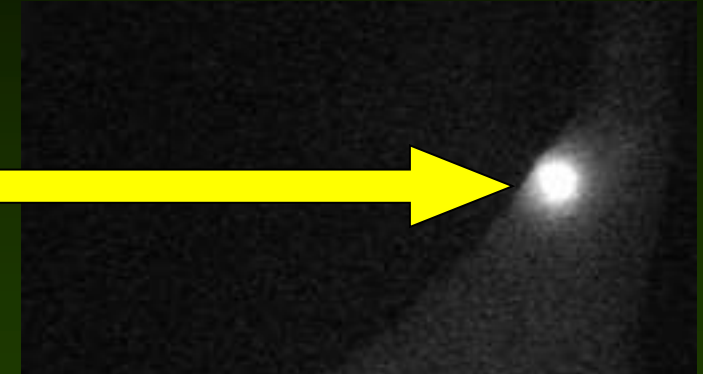


Partial resection of S2 and S3

Case 5 Examination of the resected specimen



Case 5 Examination of the resected specimen



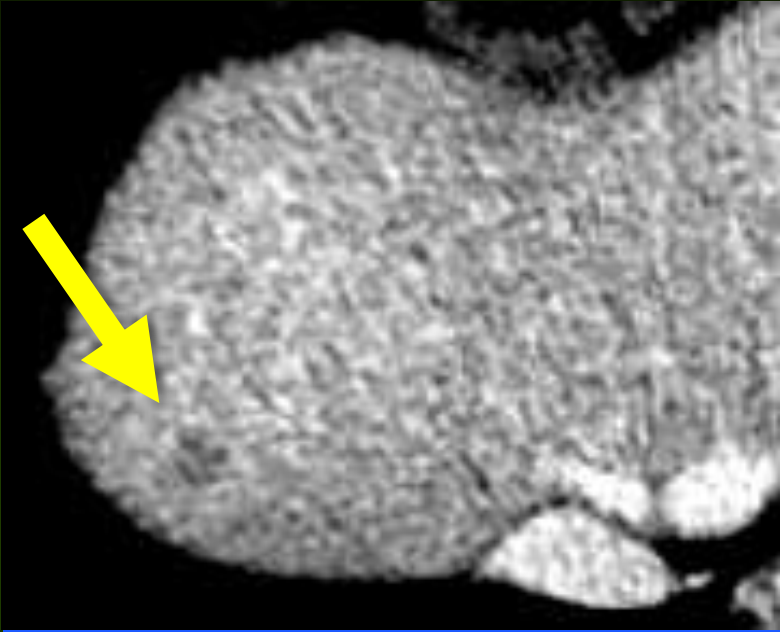
Case 6 Examination of the resected specimen



Main tumor and a daughter nodule

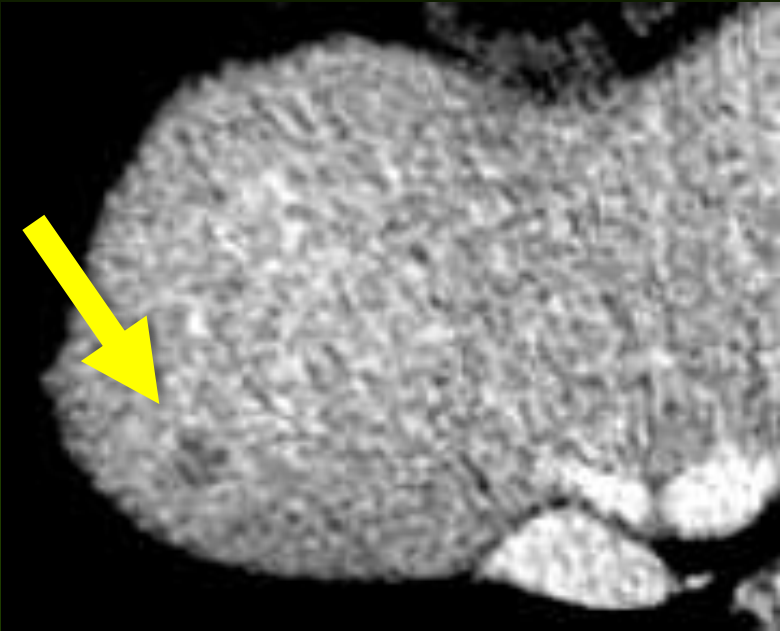
Case 7

Examination of the resected specimen



Case 7

Examination of the resected specimen



Conclusion

NTCP and OATP8 play a major role in the portal uptake of ICG in differentiated HCC cells, enabling highly sensitive identification of cancerous tissues by intraoperative ICG fluorescence imaging.

Reference

- Ishizawa T & Kokudo N. Mechanistic Background and Clinical Applications of Indocyanine Green Fluorescence Imaging of Hepatocellular Carcinoma.
Ann Surg Oncol 2013 (e-pub)

Reference

Fluorescent Imaging Treatment of Hepatobiliary and Pancreatic Diseases

Editors

N. Kokudo

T. Ishizawa



KARGER