Histopathology reporting of liver resection specimens for metastatic colorectal carcinoma:

Current practice versus set standards

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Background / Introduction

- Liver metastasis is the major complication from colorectal adenocarcinoma (adenoCa) and major contribution to patient mortality

- ~ 60% of colorectal adenoCa patients develop metastases

- In ~ 30% liver is the only site of metastasis

Background (cont.)

- Combined chemotherapy (chemoTx) regimens have markedly improved tumour response and survival rate

- ChemoTx effect can be assessed by radiological evaluation

Histology remains the best standard of assessing chemoTx tumour response

Background (cont.)

RCPath recommendations

2012 RCPath dataset for liver resection specimens for primary and metastatic carcinoma:

Same descriptors as in the colorectal dataset

2014 RCPath dataset for colorectal cancer histopathology reporting

Recording degree of tumour regression following pre-operative chemoTx **as a core data item**

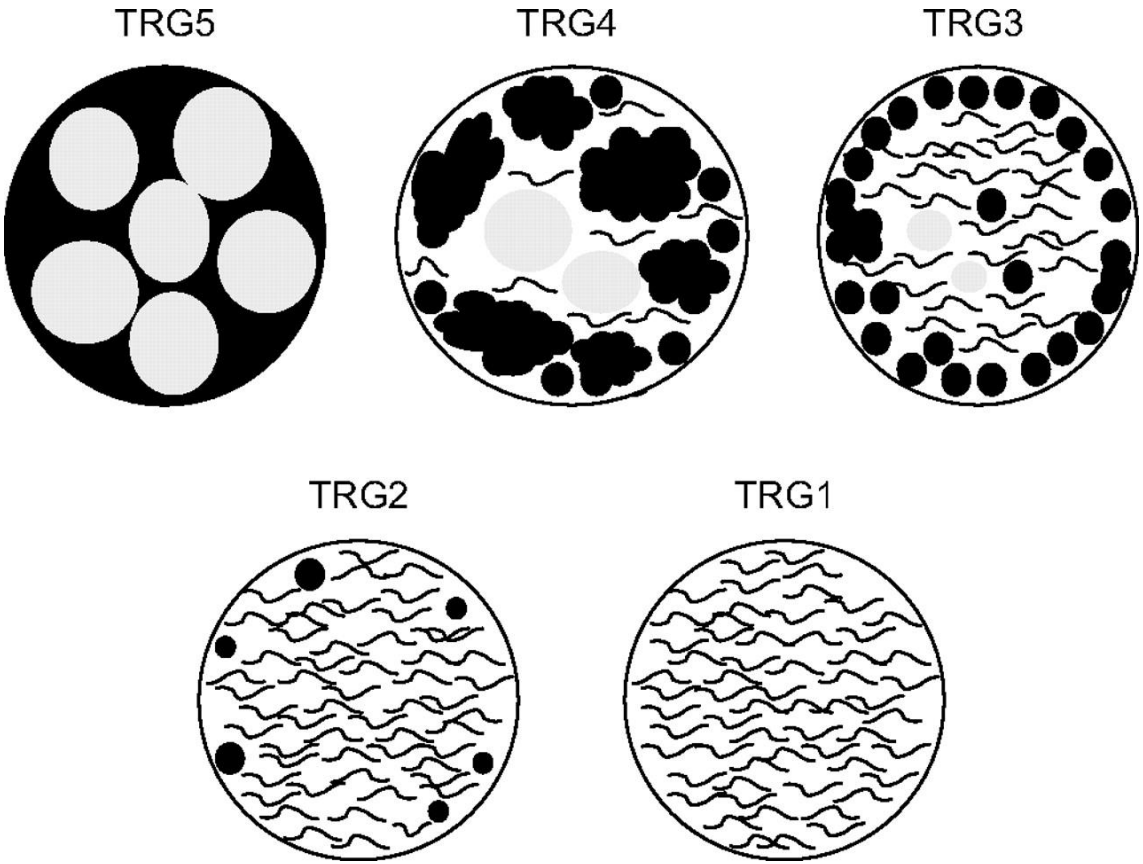
(descriptive 4-tier system)

Response to pre-operative chemotherapy: Descriptive 4-tier system (2014 RCPath dataset)

- no viable tumour cells (fibrosis or mucus lakes only)
- single cells or scattered small groups of cancer cells
- residual cancer outgrown by fibrosis
- minimal or no regression (extensive residual tumour)

Tumour regression grade (TRG)

Based on the presence of residual tumour cells and extent of tumour fibrosis:



Rubbia-Brandt L et al. Ann Oncol 2006

Annals of Oncology

Background (cont.)

- ChemoTx regimens may affect non-neoplastic liver parenchyma causing:

✓ steatohepatitis

✓ sinusoidal endothelial injury

✓ nodular regenerative hyperplasia (NRH)

✓ other side effects

Rubbia-Brandt L *et al.* Annals of Oncology 2004

Background liver: Neoadjuvant therapy effects

- Varies with the agent used
- Oxaliplatin may induce SOS (50% of patients)
- Irinotecan may contribute to steatohepatitis
- Sinusoidal obstruction syndrome

nodular regenerative hyperplasia

portal hypertension

RCPath liver resection specimens dataset 2012

Sinusoidal obstruction syndrome (SOS)

- Microvascular/sinusoidal injury
- Also called **toxic microvascular injury**
- Previously known as veno-occlusive disease (VOD)

Aetiology

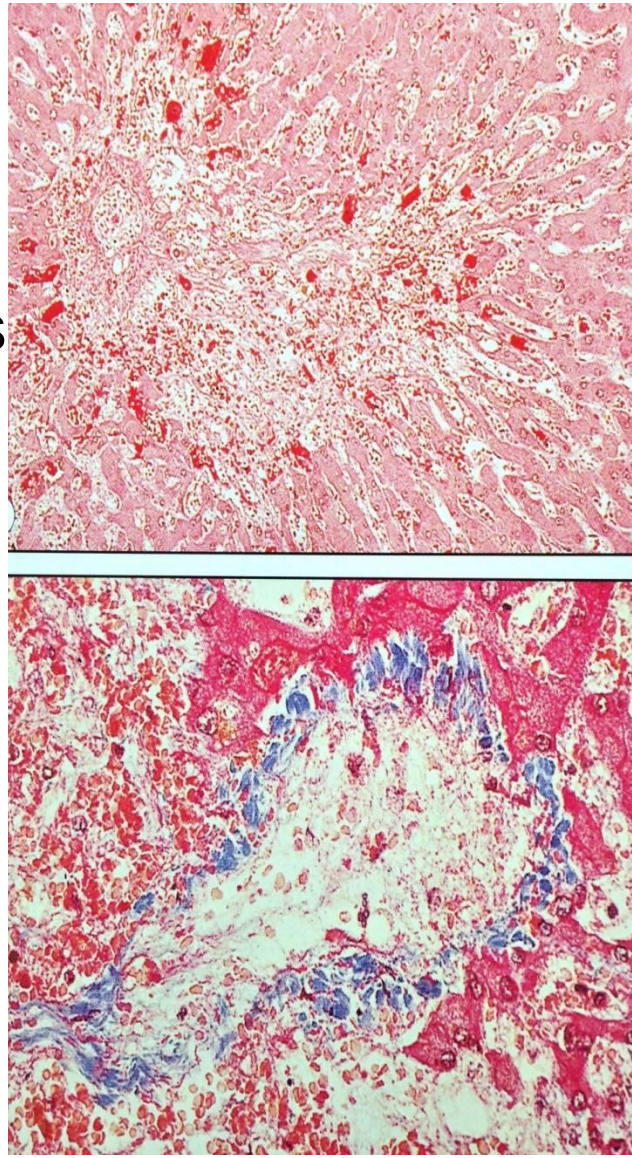
- **chemoTx effect**
- ischaemic
- congestive
- infiltrative injuries

SOS (cont.)

- sinusoidal oedema and haemorrhage
- fibrin deposition
- severe sinusoidal congestion => necrosis
- healing with concentric/eccentric intimal fibrosis/ fibrous obliteration
- zone 3 atrophy and sinusoidal fibrosis

Late features:

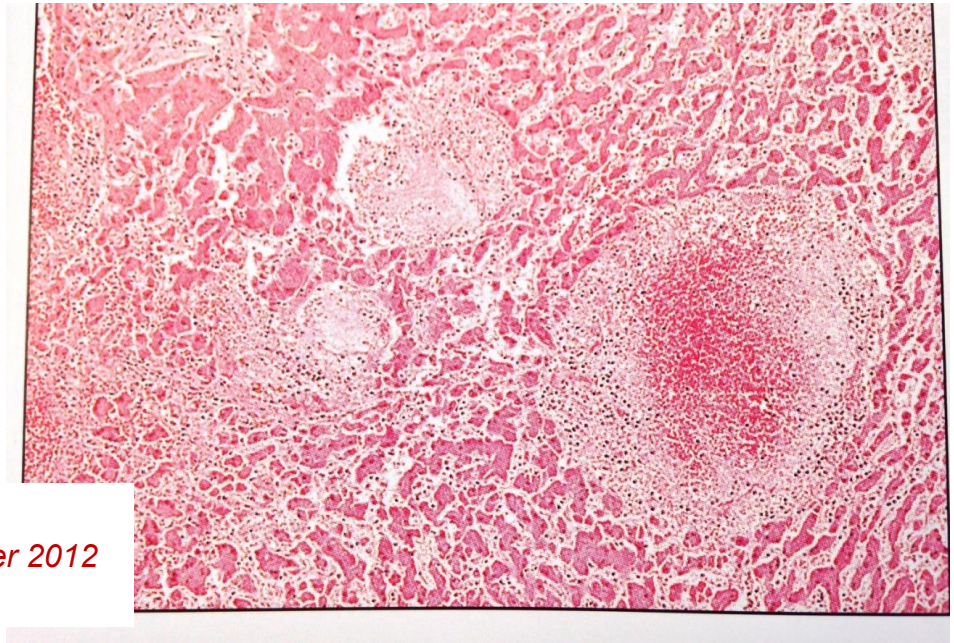
- cirrhosis (congestive type), relative sparing of portal tracts
- regenerative nodules (NRH)



Burt A, MacSween's pathology of liver 2012

Peliosis

- Cystic blood-filled spaces
- Rupture of reticulin fibres
- Randomly distributed
- D.D.
  - evacuation of hepatocyte plates seen after **zona**l hepatocellular dropout but **without loss of reticulin fibres**
  - Sometimes confused with extreme sinusoidal dilatation



Burt A, MacSween's pathology of liver 2012

Background liver: Neoadjuvant therapy effects

2012 RCPath dataset for histopathology reporting of liver resection specimens for primary and secondary colorectal adenocarcinoma:

- Assessment of **presence and severity of background liver changes**

- **Qualitative estimate of the severity of chemotherapy-related effects** in the background liver parenchyma (although changes may be heterogeneous)

Aims of the audit

- Evaluate if required standards were achieved in routine histopathology reporting of liver resection specimens for colorectal adenoCa metastasis

2009/2010 vs 2013 (post 2012 RCPath dataset)

- Document % reported cases in which gross and microscopic description proforma were used

- Document % cases in which the gross/microscopic items were mentioned/not mentioned in the report

Aims of the audit (cont.)

- Collect information on post-chemoTx effect in hepatic resection specimens for colorectal adenoCa liver metastasis

- **2009/2010 vs 2013:** assess completeness of documentation regarding sinusoidal endothelial injury and other chemoTx effects in the non-neoplastic background liver tissue

Standards used

- Local proforma for macroscopy and histology reporting
- 2012 RCPath Dataset for histopathology reporting of liver resection specimens for primary and metastatic carcinoma
- Histological grading of tumour response to chemotherapy and grading of chemoTx-related injury in background liver

Audit methods

Time period audited:

- 12 months (all cases in 2013):

  Surgical specimens of liver resection for metastatic colorectal adenocarcinoma reported in RVI were included in the audit (n=60)

- Randomly selected cases of primary colorectal adenoCa with liver metastasis from years 2009 and 2010 (n=26)

Data documented

Macroscopic details:

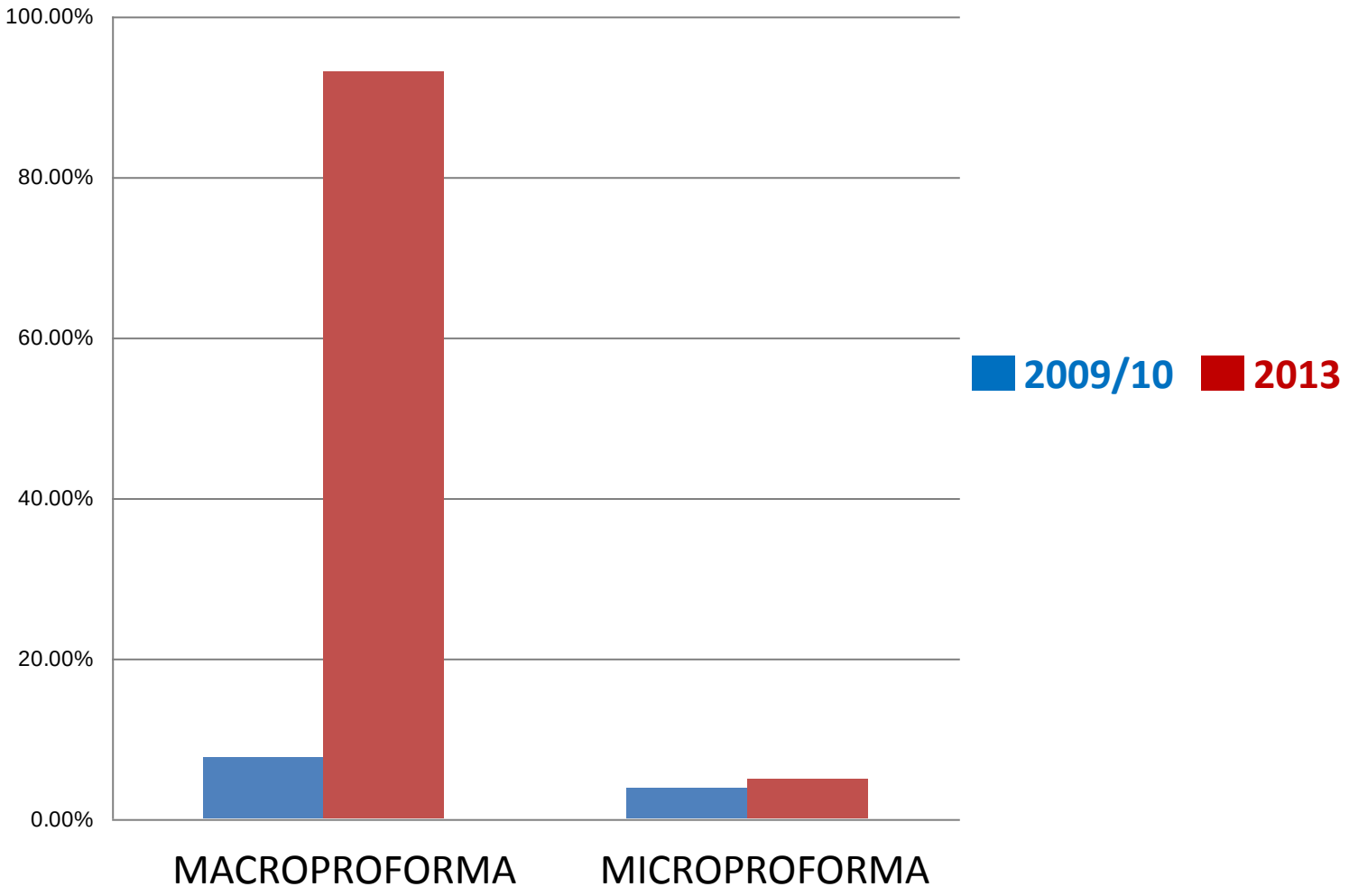
- specimen type, weight, dimensions
- surgical resection area size/appearance
- liver capsule
- tumour number/size/site/distance to margin
- macroscopic vascular invasion
- vascular margin
- background liver description
- background tissue block
- lymph nodes

Data documented (cont.)

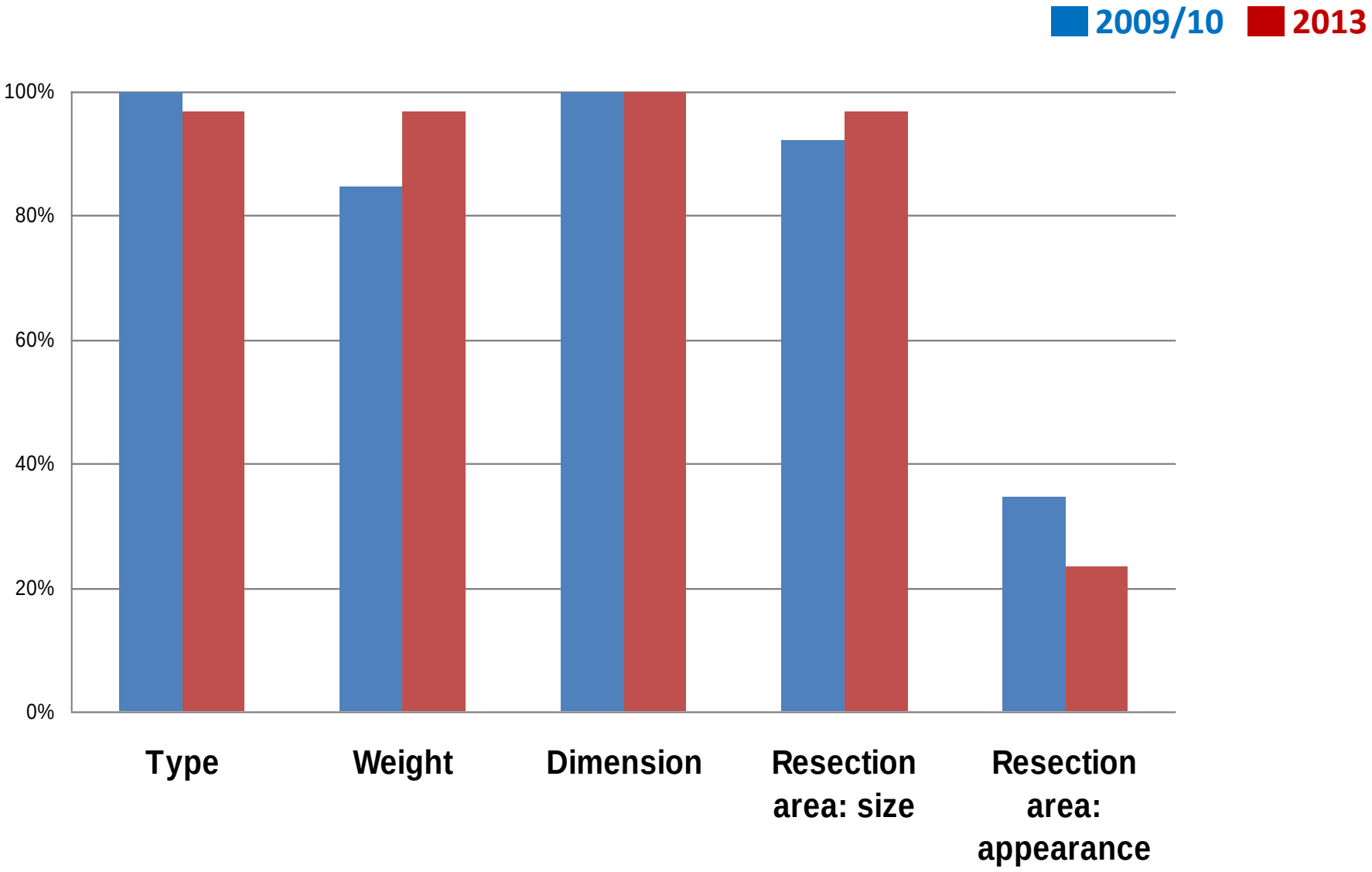
Microscopic details:

- **Tumour**: histological type, differentiation, fibrous capsule, invasive margin, lymphocytic infiltrate
- **Invasion**: lymphatic, vascular, perineural, bile duct colonization,
- **Post-chemoTx** (PCE), extent of PCE
- **Tumour regression grade**
- **Satellite lesions**
- **Margins**
- **Lymph node status**
- **Background liver:** steatosis, steatohepatitis, fibrosis, NRH, sinusoidal obstruction syndrome, peliosis

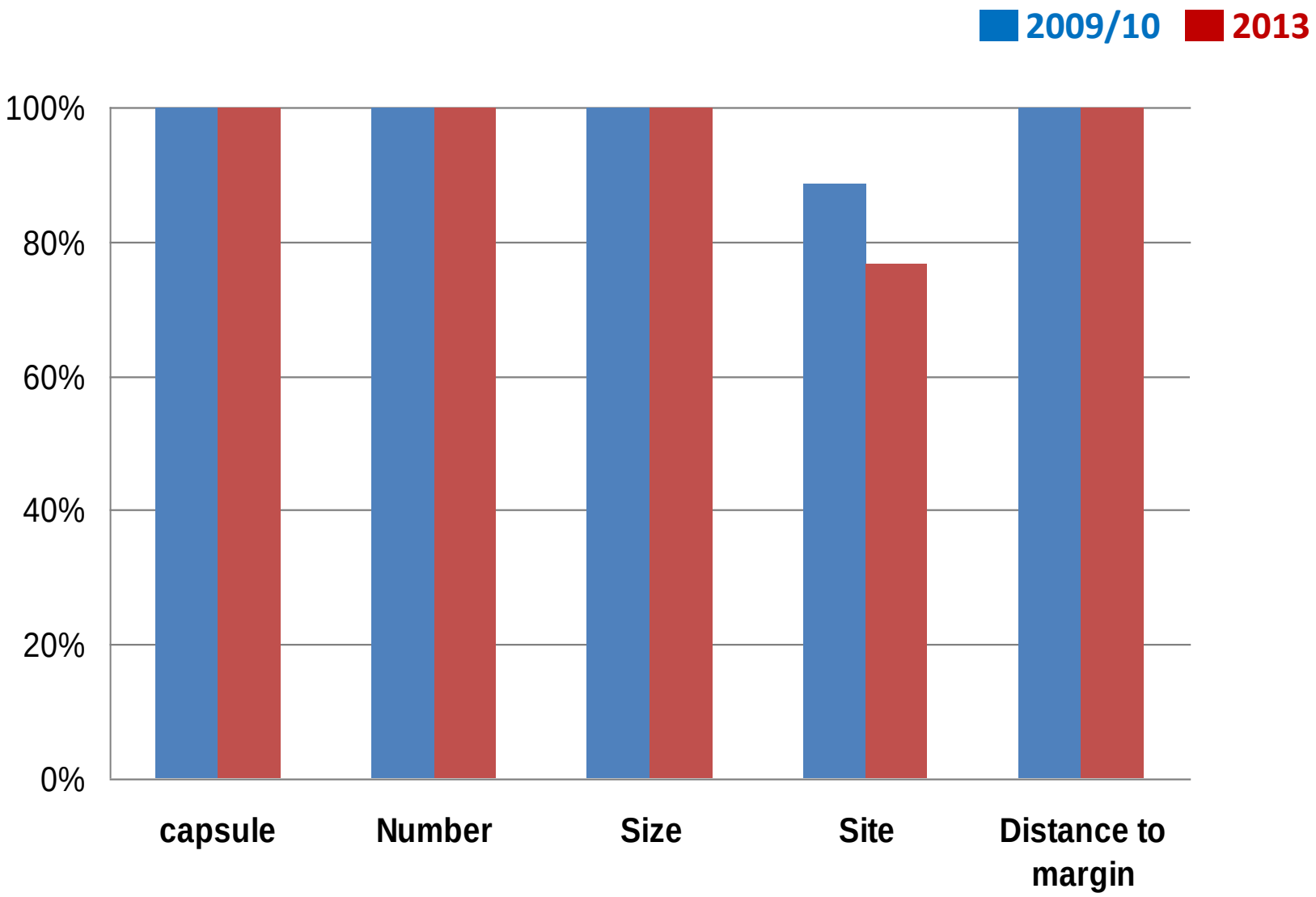
Results: Use of proforma



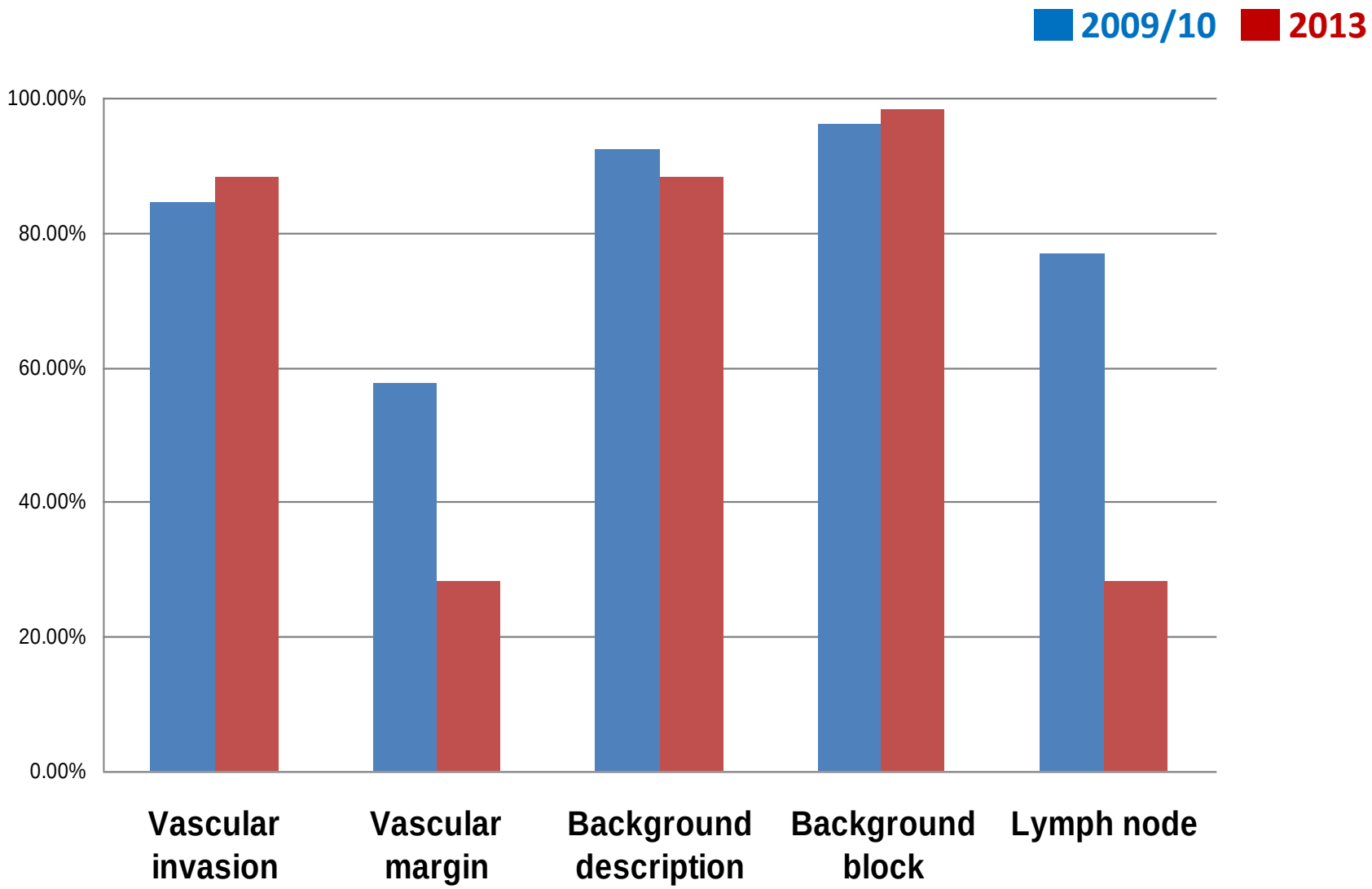
Results: Specimen details



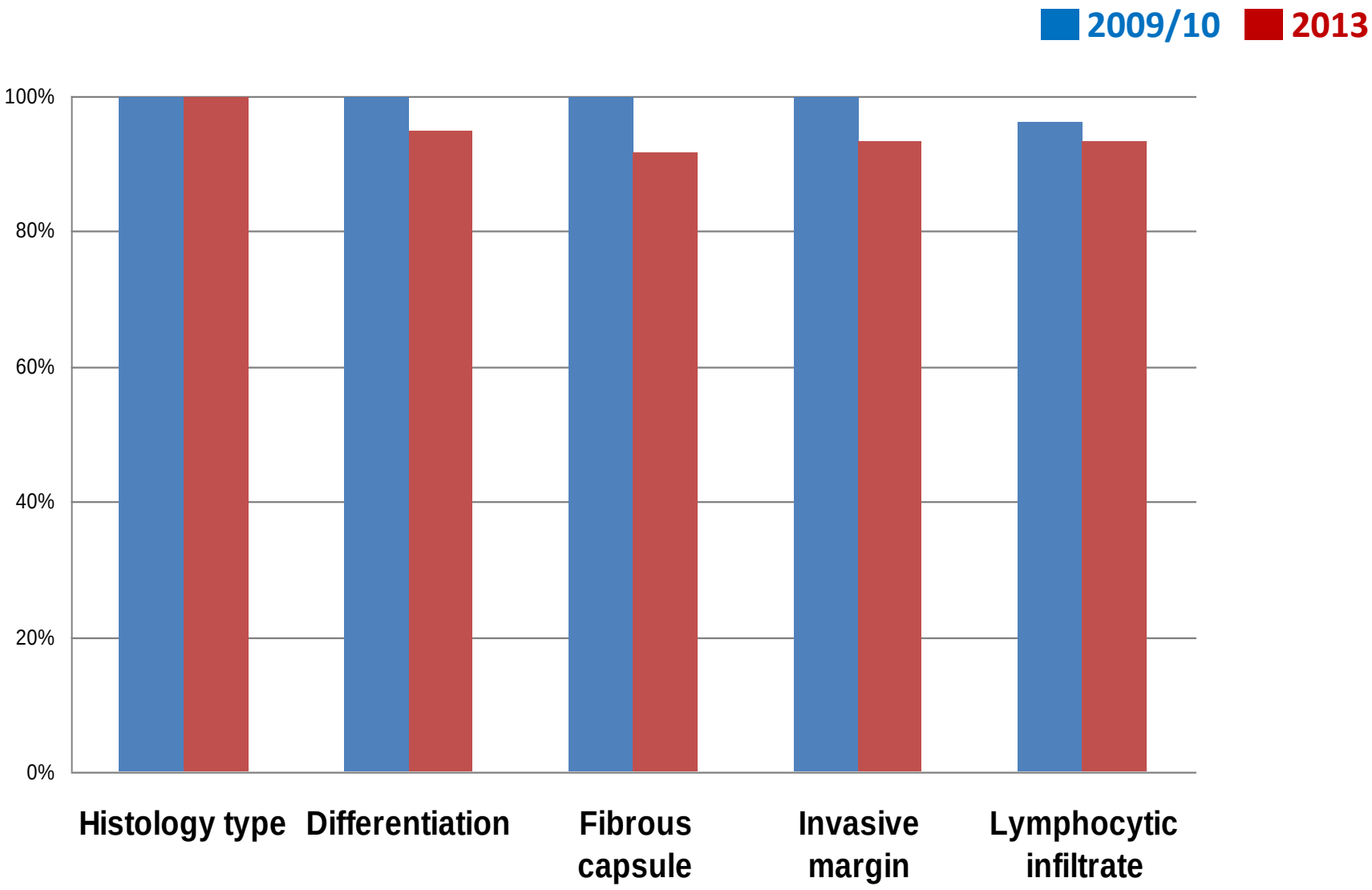
Results: Macroscopic tumour details



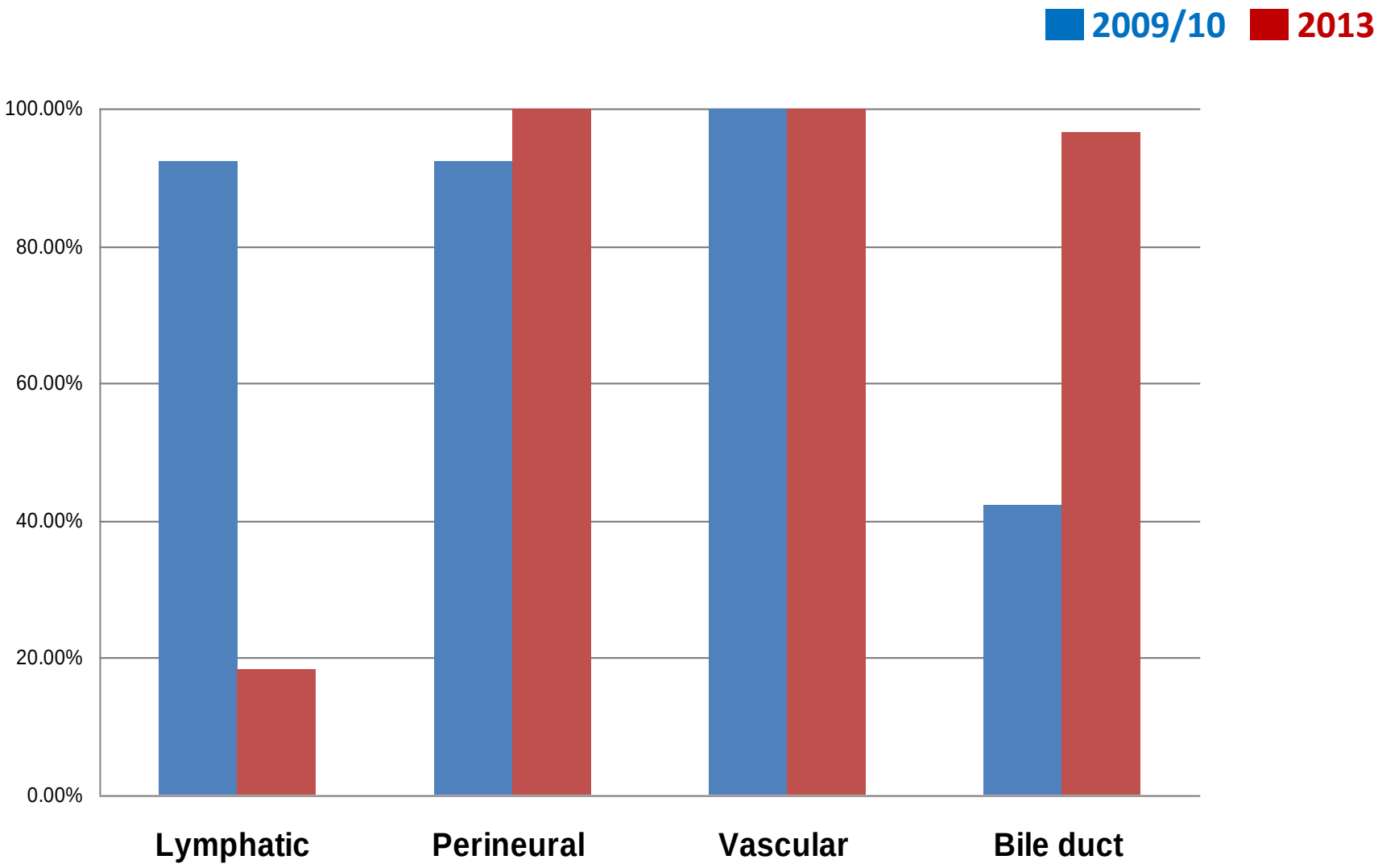
Results: Macro, other details



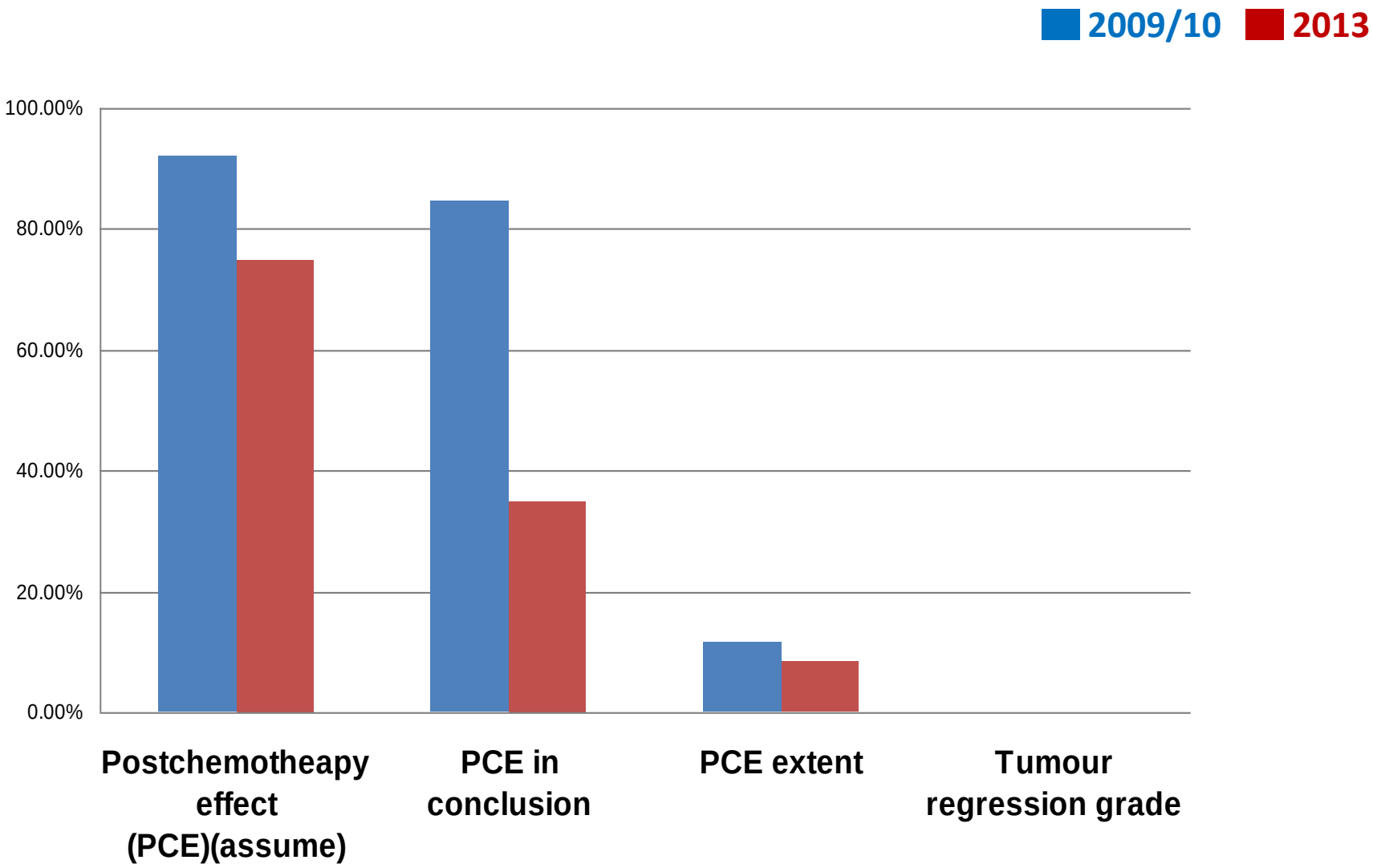
Results: Tumour histology



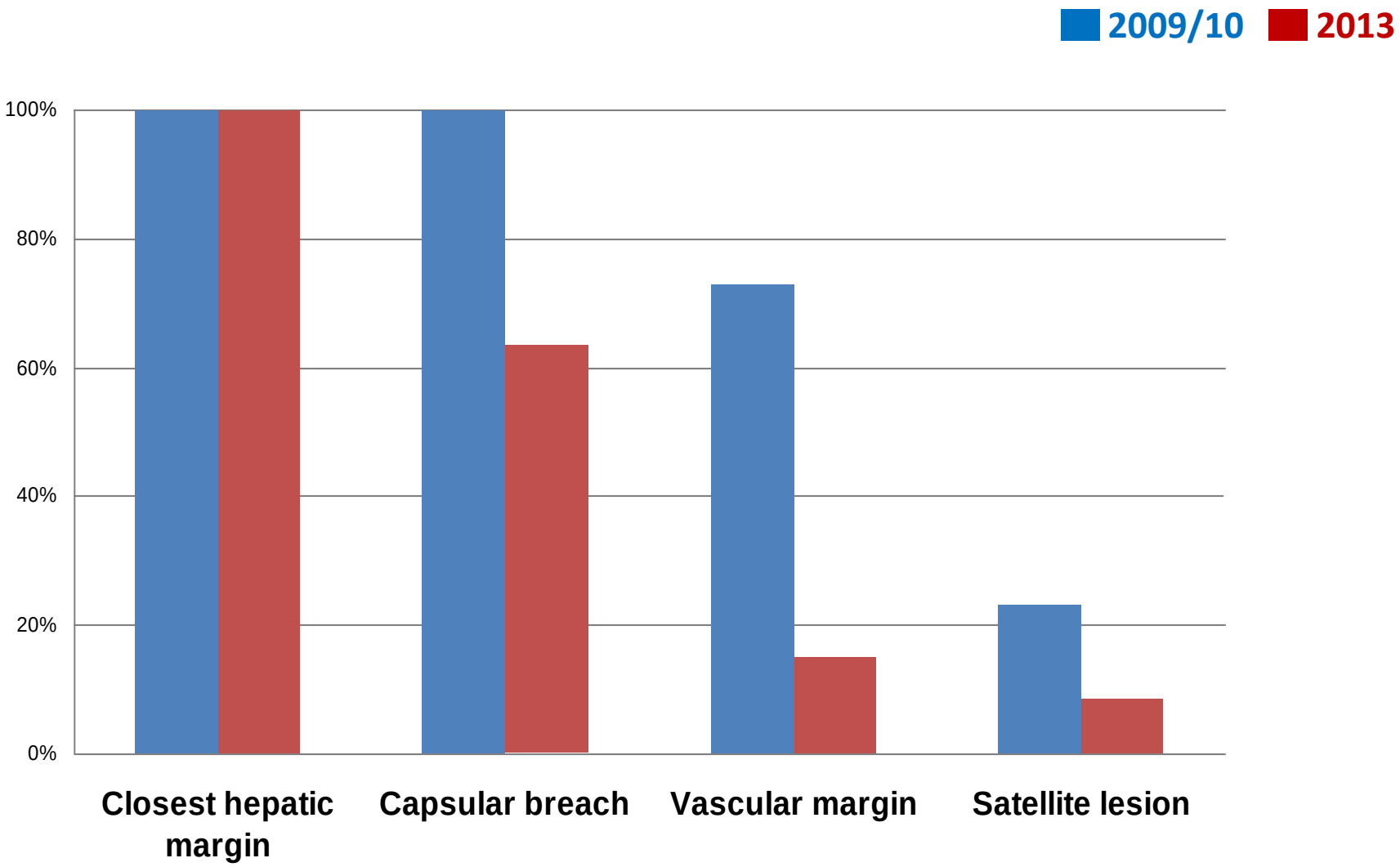
Microscopy: Invasion



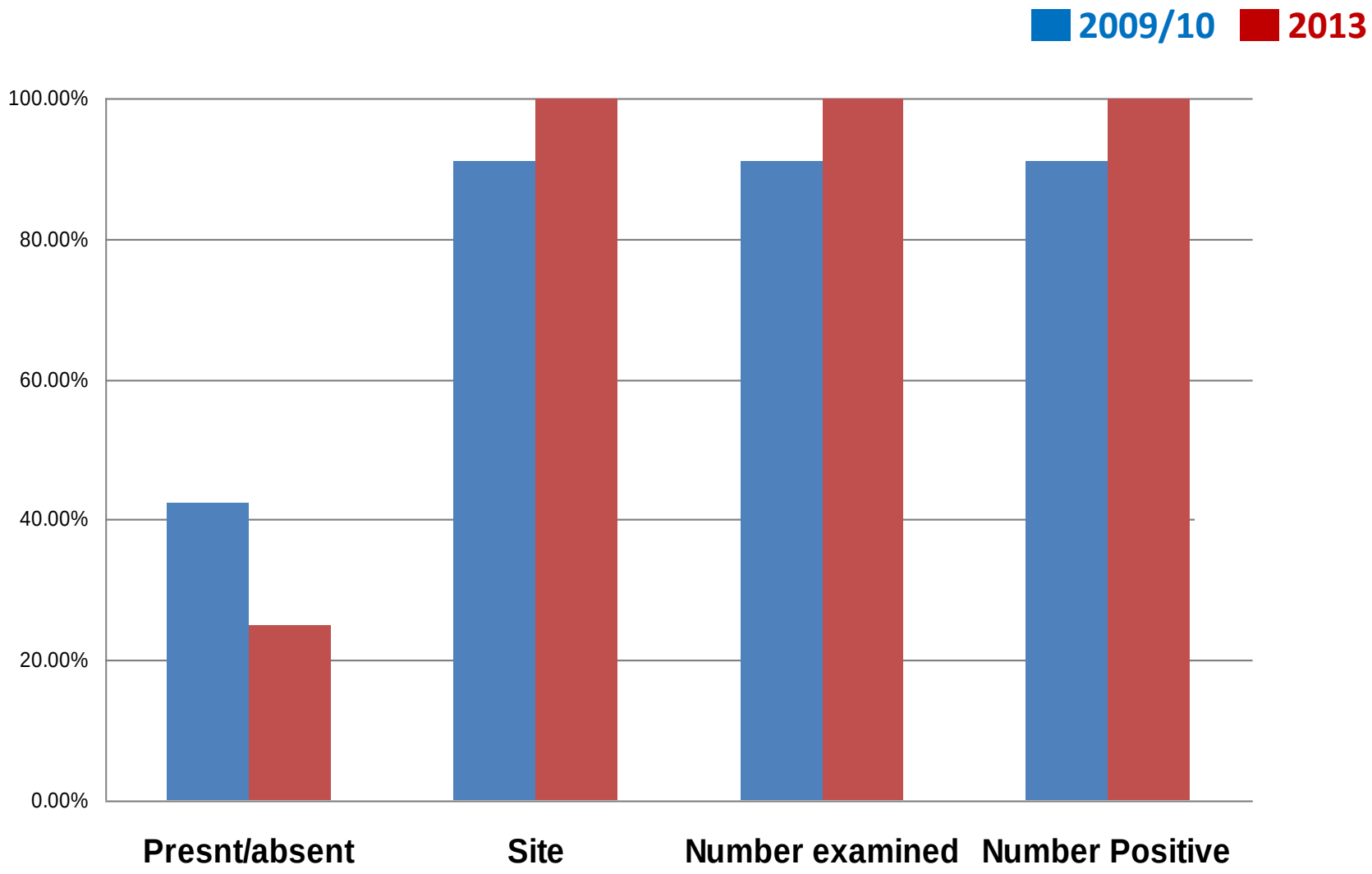
Microscopy: ChemoTx effect



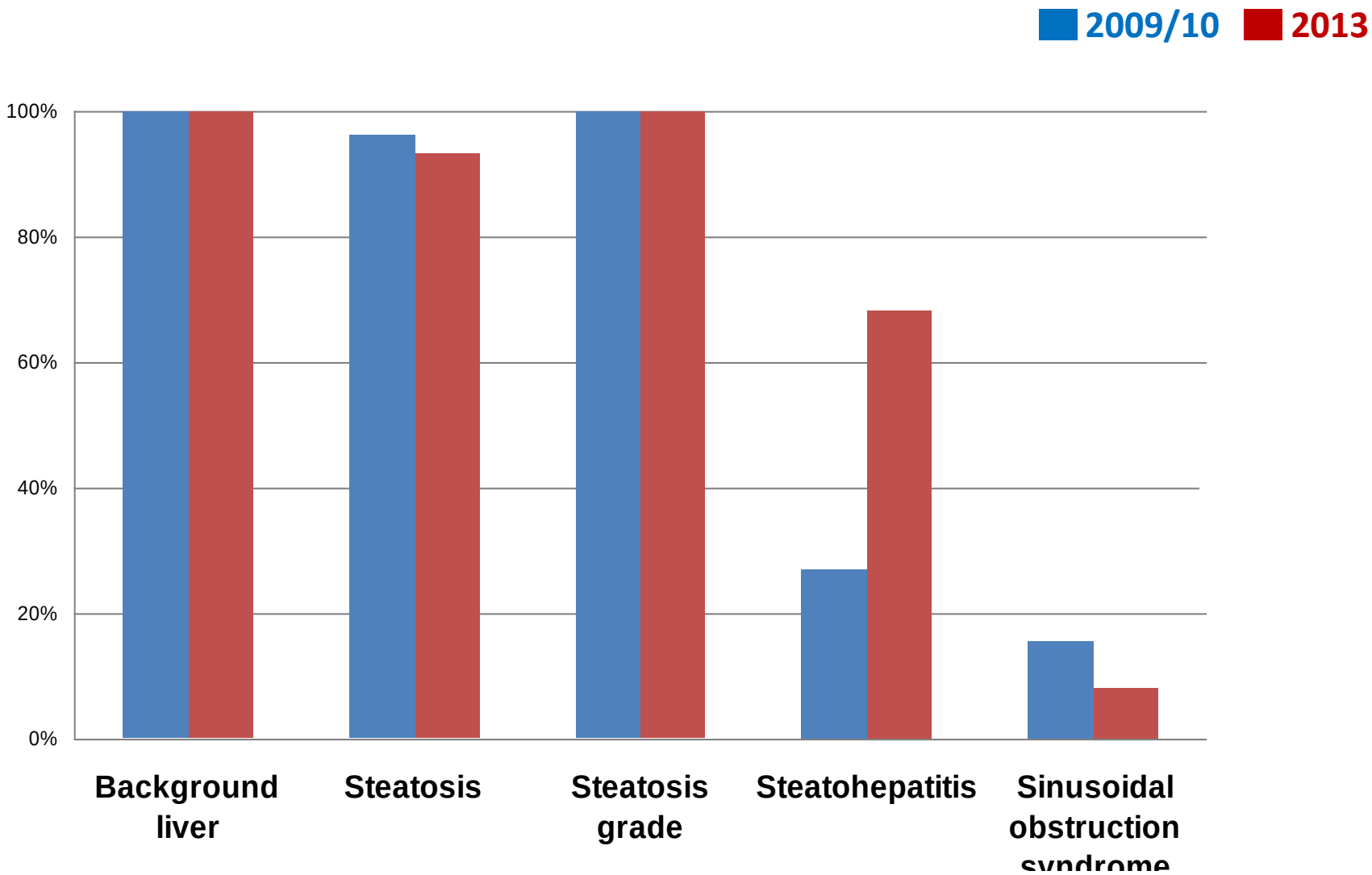
Microscopy: Margins



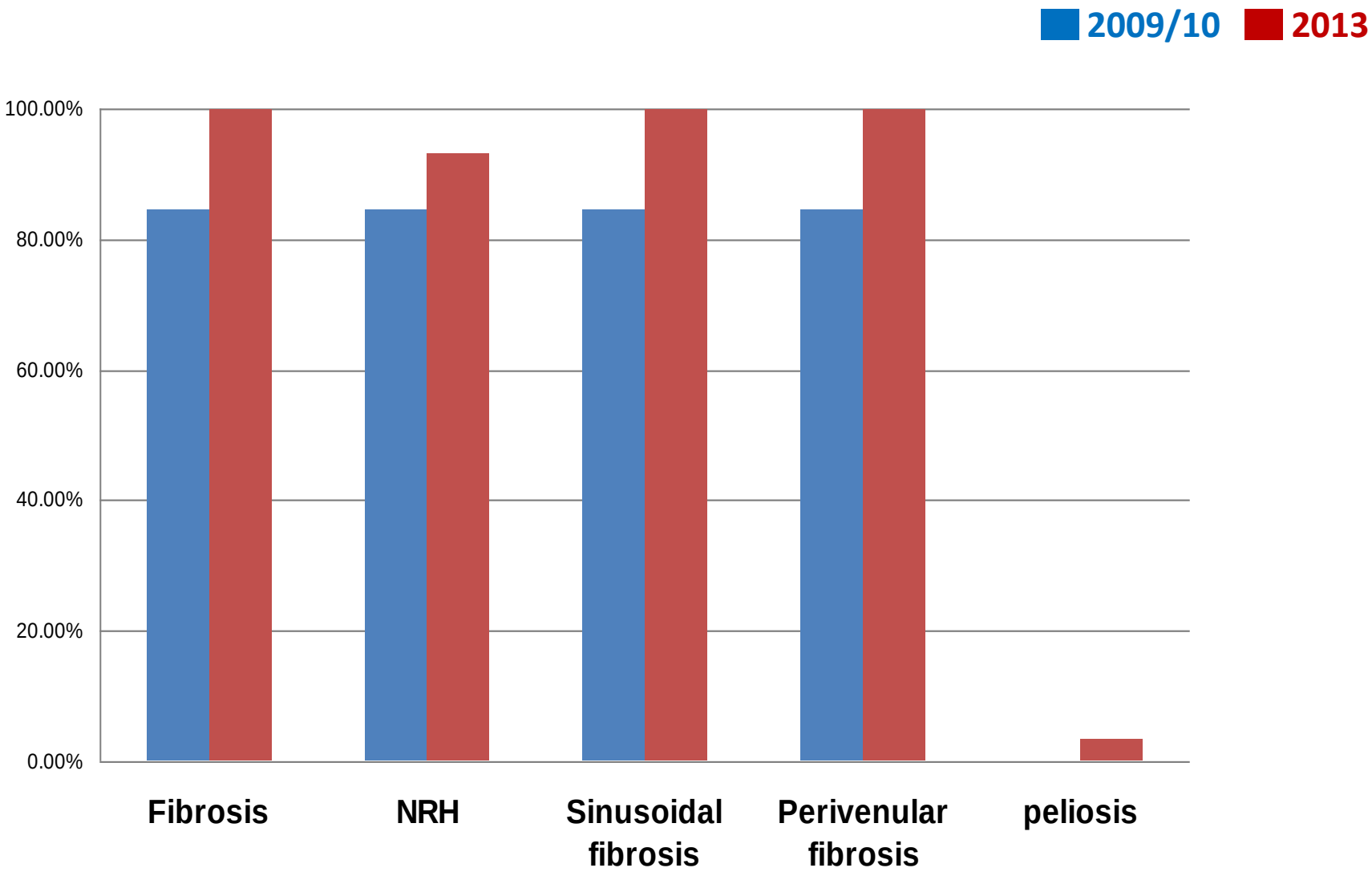
Microscopy: Lymph nodes



Microscopy: Background liver



Microscopy: Background liver



Conclusions

- **Many items (gross and microscopic) were mentioned in >90% (some items=100%) of cases in both groups.**
- **Use of macroproforma significantly improved** in 2013 vs 2009/2010.
- The **microproforma was rarely used**
- **Negative details not adequately mentioned** in macro- and microscopic descriptions (both groups)
- **Inadequate documentation of post-chemoTx effect** on the tumour (both groups)
- **Tumour regression not graded** (both groups)
- **Post-chemoTx effects in non-neoplastic liver parenchyma not adequately documented** (both groups)

Recommendations for histopathology reporting liver resection specimens for colorectal adenoCa metastasis

- **Adherence to the use microproforma and macroproforma**
- **Reporting of negative findings**
- **More detailed description of tumour post-chemoTx effect**

  Use of a tumour regression grading system to semi-quantitate post-chemoTx effect

- **Include in the microproforma more detailed description of chemoTx effects in the background liver parenchyma**

Action plan

- **Feedback audit results** to histopathology consultants, trainees and advanced practitioners

- **Re-audit** after the implementation of the above recommendations to measure degree of improvement

References

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2. Adam R, et al. Rescue surgery for unresectable colorectal liver metastases downstaged by chemotherapy: a model to predict long-term survival. *Annals of Surgery* 2004; 240 (4):644–657.

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http://www.rcpath.org/Resources/RCPath/Migrated%20Resources/Documents/G/G050_LiverDataset_Jun12.pdf

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THANK YOU