69ste Geneeskundige Dagen van Antwerpen

2014

Symposium Gastro-intestinale Oncologie

Rol van de chirurgie bij levermetastasen: hoever kan je gaan in curatief opzet ?

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Dienst Hepatobiliare, Transplantatie en Endocriene Heelkunde

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Sterk verbeterde therapeutische opties voor CRLM tijdens laatste decade

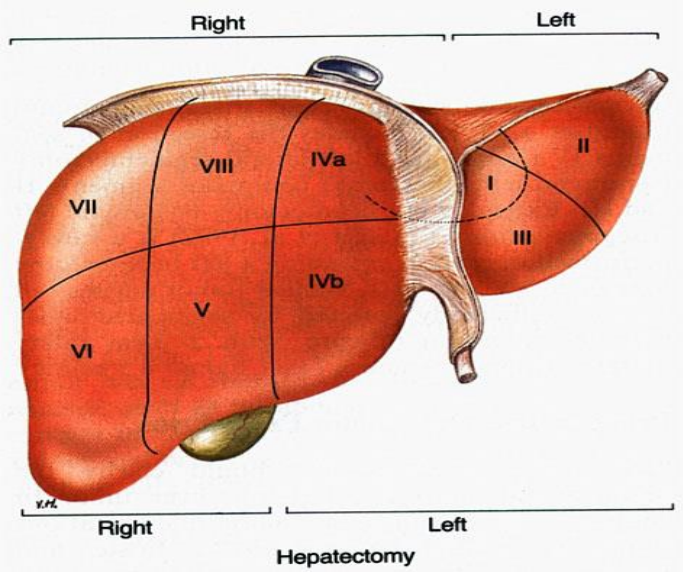
- Morfologische én functionel imaging (MRI, PET, PET-CT,…)

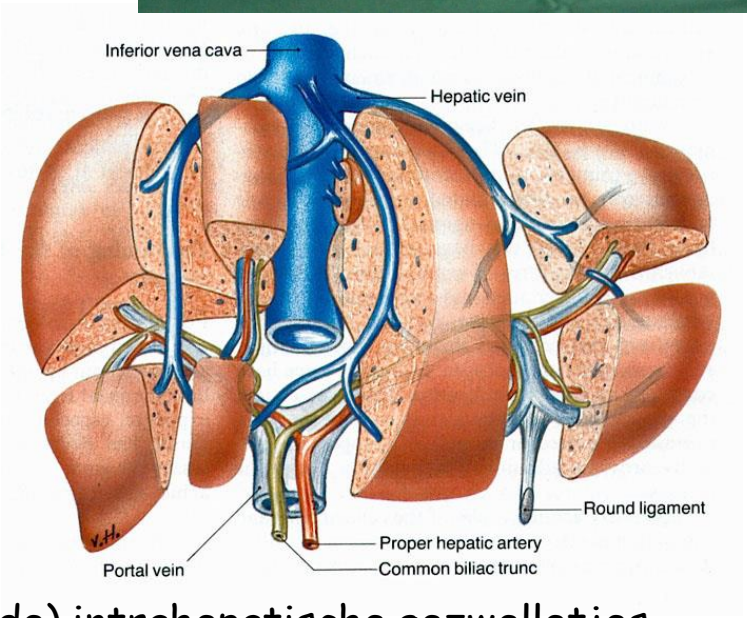
  → verbeterde selectie

- Chemotherapie : potentie / tolereerbaarheid / arsenaal
- Chirurgie :
  - Verbeterde resectabiliteit
  - Veiligere chirurgie /anesthesie
    - IOUS
    - Laag centrale veneuze druk anesthesie
    - Accurate parenchym dissectie technieken
    - Inflow occlusie and totale vasculaire occlusie mogelijkheden/bypass

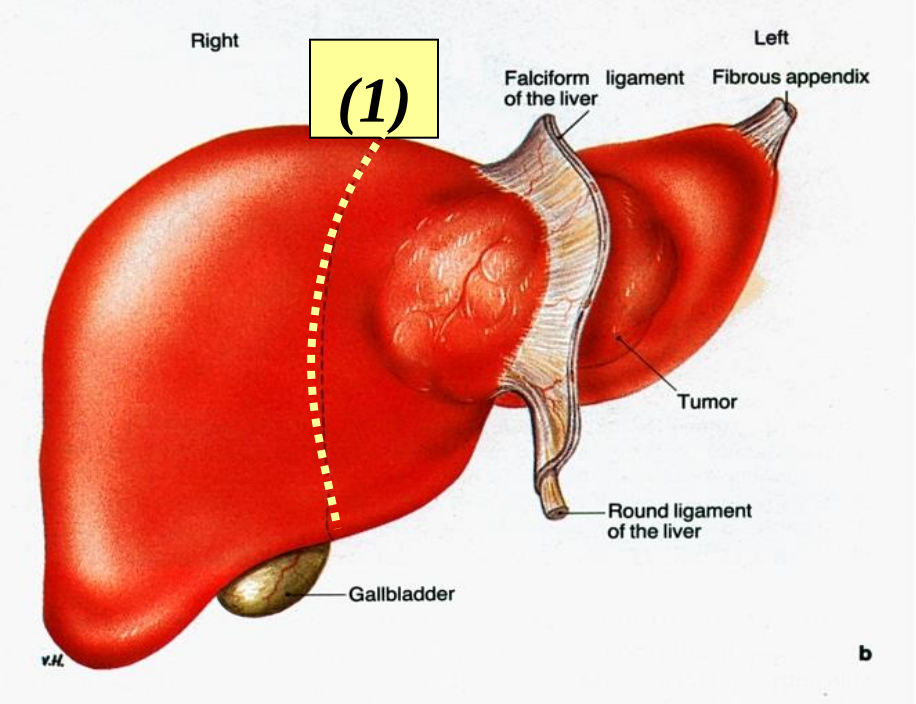
      → invloed van technieken uit de levertransplantatie

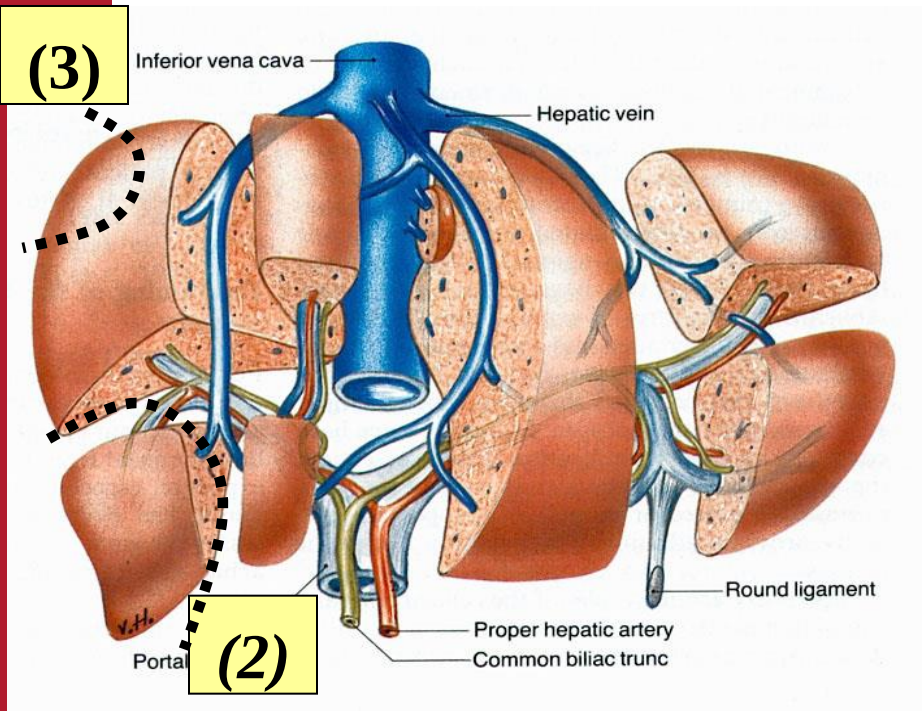
Geen hedendaagse leverchirurgie zonder intraoperatieve US





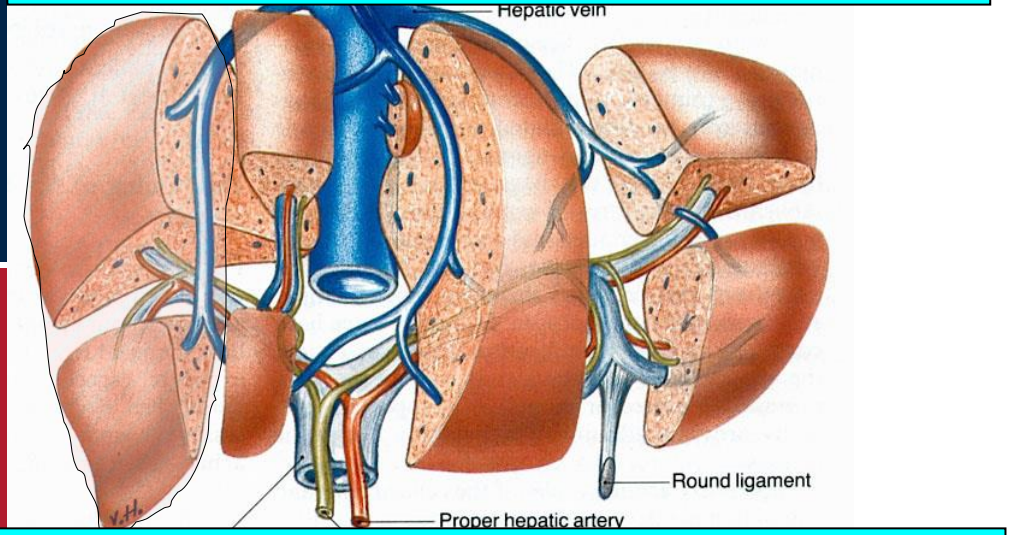
- herkenning van intrahepatische tumoren
- identificatie van kleine (tevoren onbekende) intrahepatische gezwelletjes
- relatie tumor – galwegen en vasculaire structuren
- identificatie segmentele anatomie
- adequate tumorgrenzen bij resectie



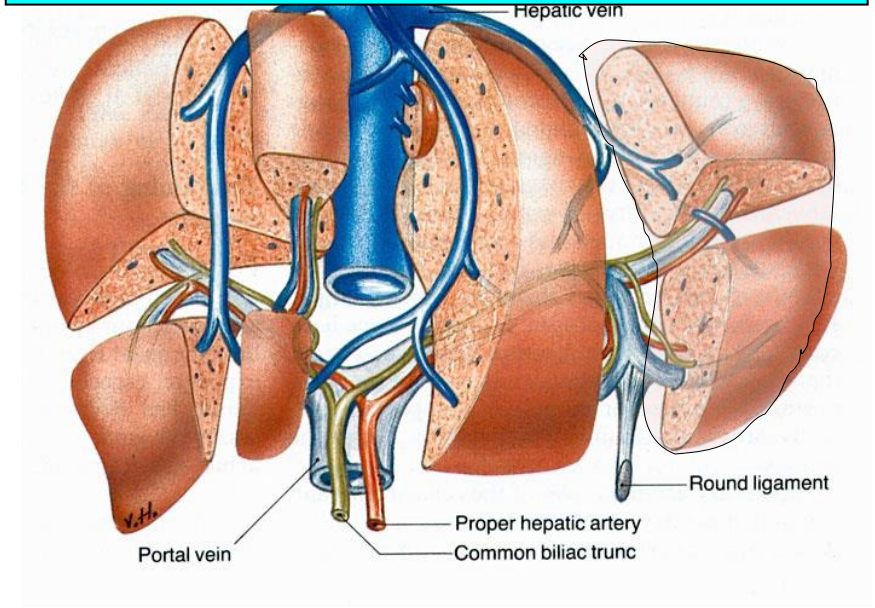


- hemi-hepatectomie (1):
  - linker
  - rechter
- segmentectomie (2)
- atypische resectie (3)
- *of combinatie !*

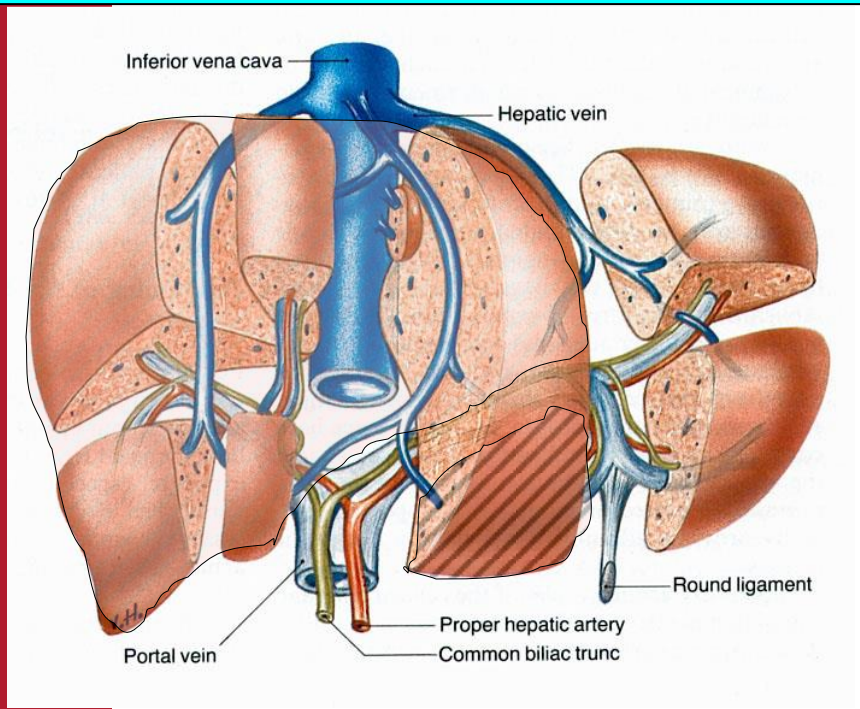
Rechter laterale sectoriectomie



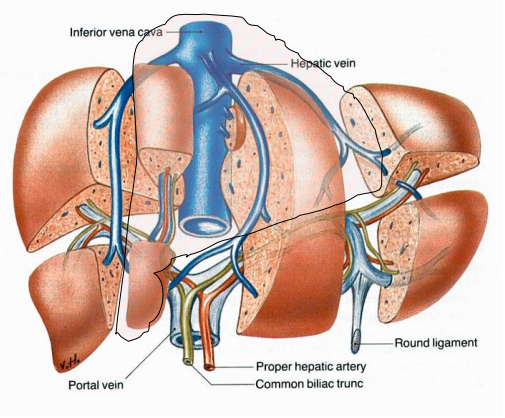
Linker lobectomie



Rechter lobectomie /“extended right hepatectomy”



Centrale hepatectomie



Impact van de anesthesist op de hemostase

Stollingsfactoren of bloedplaatjes bijgeven
Centrale veneuze druk laag houden
Bloedverlies recupereren ("Cell-saver")
Snel bloedtransfusie ("Rapid Infusion System")
Stolling perop bepalen (thrombo-elastogram)

Belangrijk ?

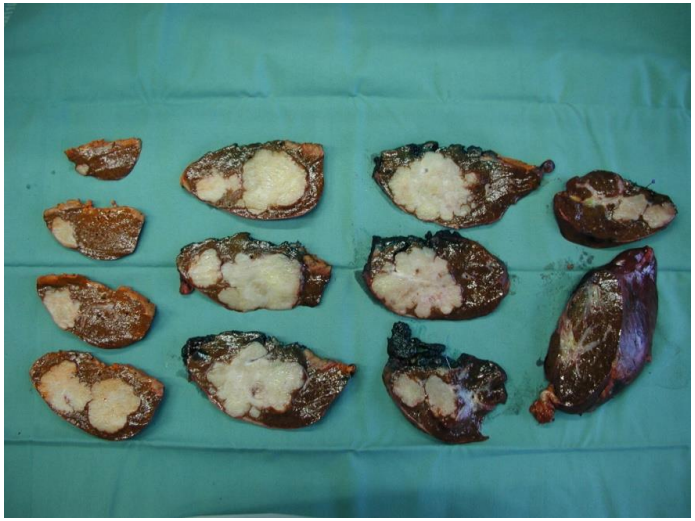
Reductie *operatieve mortaliteit*

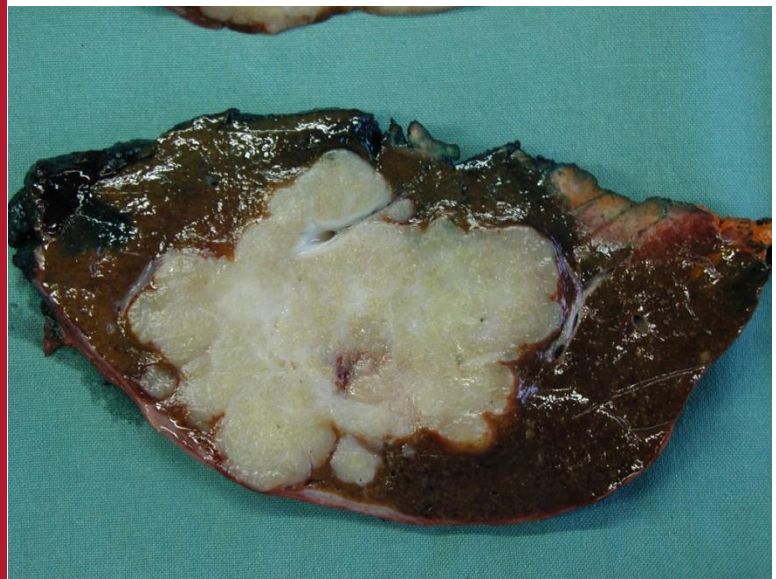
Minder onderdrukking van *immuniteit*:

- minder infecties
- minder tumorrecidief

Betere lange termijnsoverleving

Peroperatieve beoordeling van snijranden: heeft de chirurg een RO of R1 ?

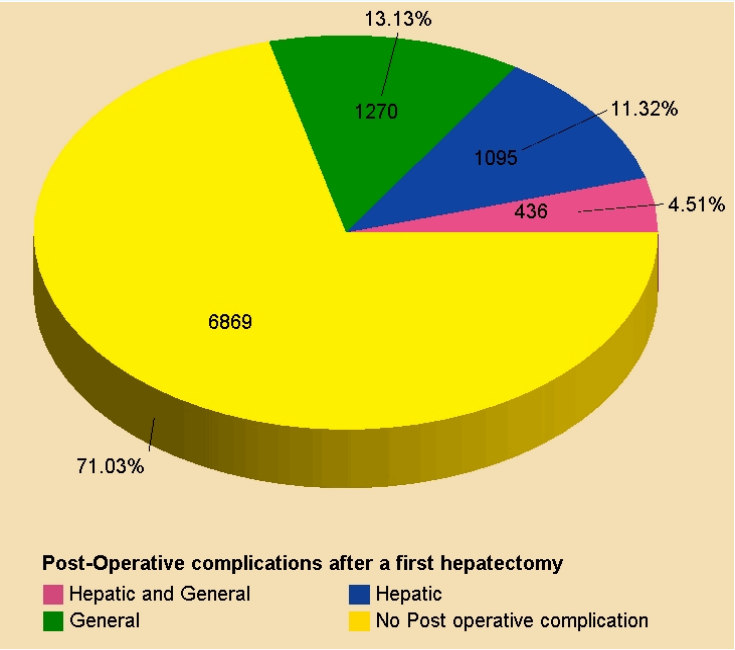


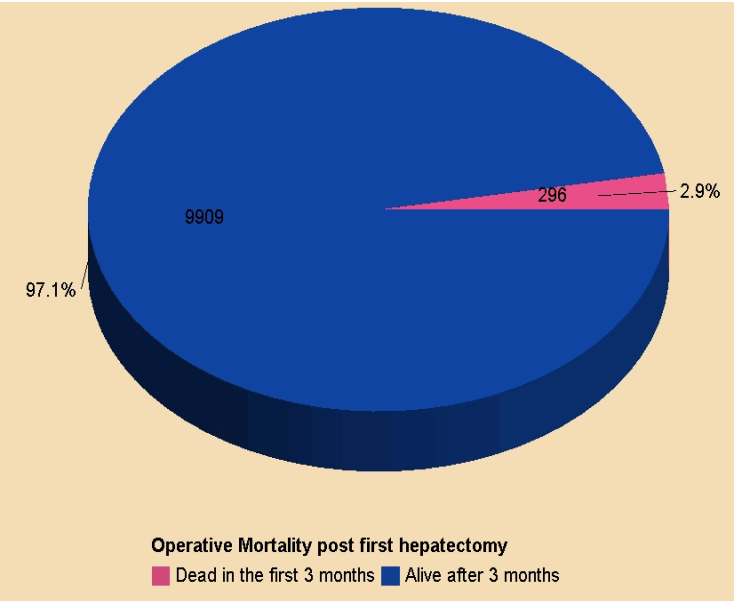


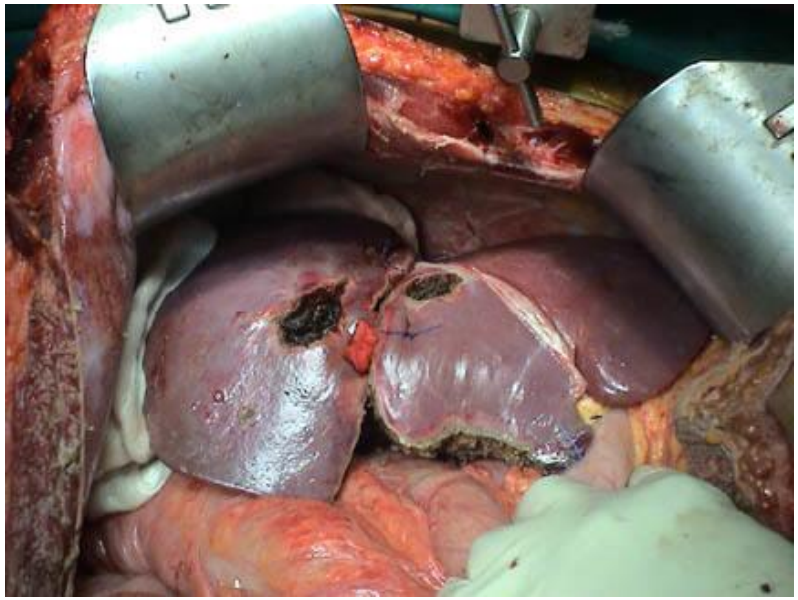
Zo nodig re-resectie tot RO bekomen wordt

ROL VAN DE PATHOLOOG

Morbiditeit en mortaliteit na CRLM chirurgie – anno 2010



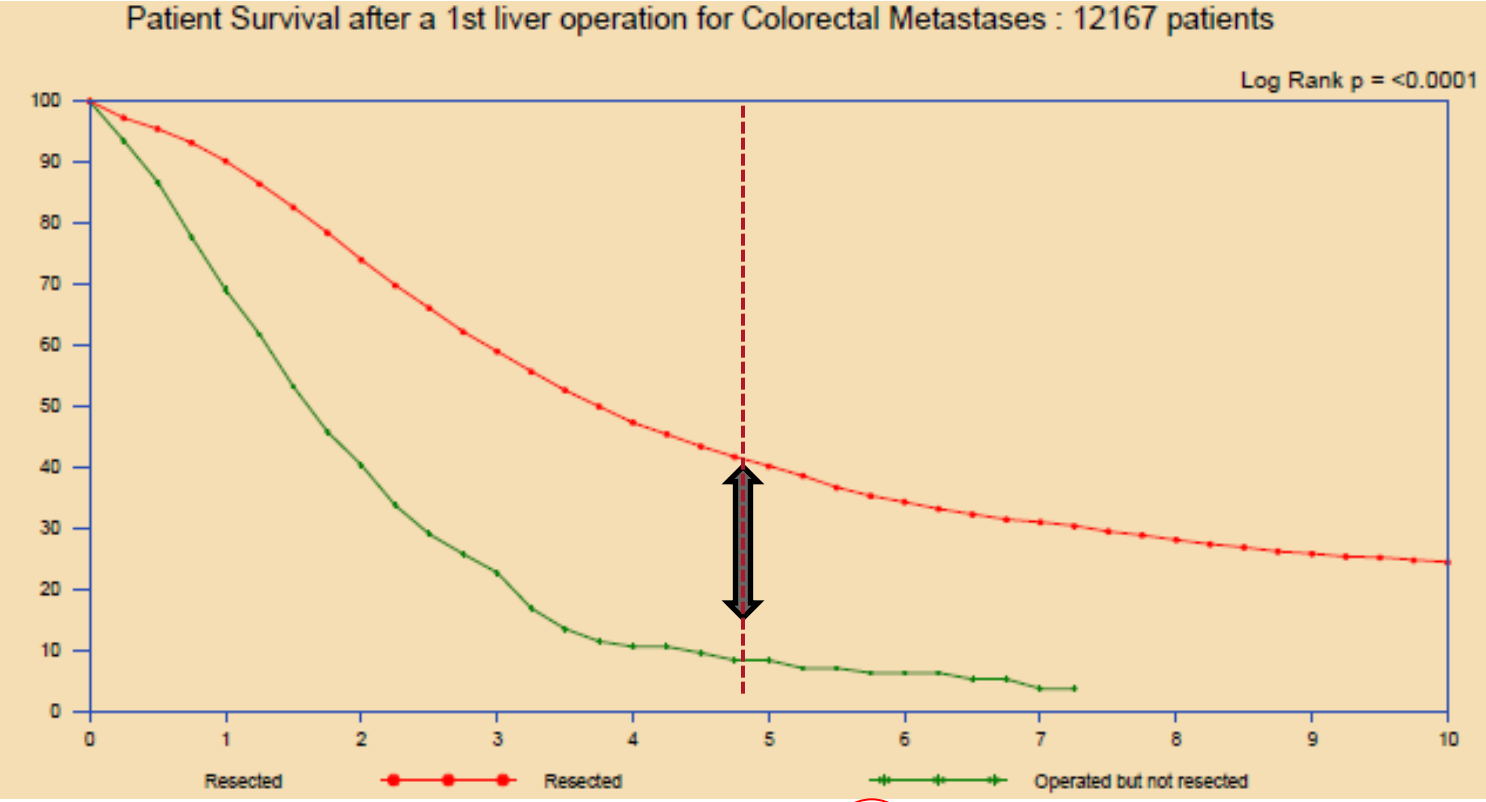




Colorectale Lever Metastasen (CRLM)

- 15-25 % synchroon 35-45 % metachroon
- 20-30 % metastasen alleen in de lever
- 15-20 % primair reseceerbaar, terwijl 10-20 % pas secondair reseceerbaar worden
  → dus 30 (- 40 % ?) totale reseceerbaarheid
- RO – Chirurgie = momenteel (bijna) enigste kans op genezing

CRLM resectie = potentiële genezing van CRLM



Survival %

Resected	1 yr	2 yrs	3 yrs	4 yrs	5 yrs	6 yrs	7 yrs	8 yrs	9 yrs	10 yrs
Resected	90%	74%	59%	47%	40%	34%	31%	28%	26%	24%
Not res.	69%	40%	23%	11%	8%	6%	4%			

Livermetsurvey

Universiteit Antwerpen

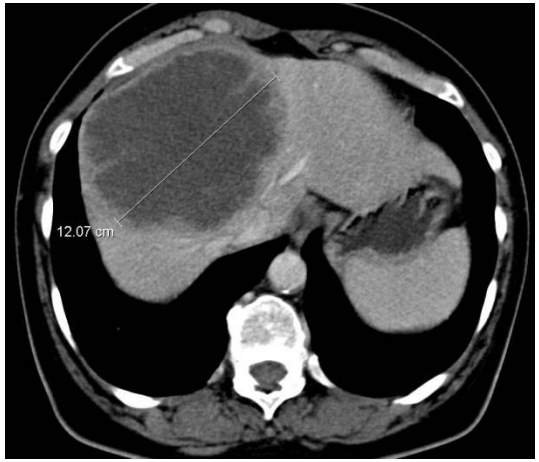
UZA kennis / ervaring / zorg

Reseceerbaarheid CRLM

Klassieke criteria

- Marge 1cm
- Aantal M+
- Max diameter M+
- Extrahepatische ziekte

= *"what has to be removed"*



Reseceerbaarheid CRLM

Klassieke criteria

- ~~Marge 1cm~~
- ~~Aantal M+~~
- ~~Max diameter M+~~
- ~~Extrahepatische ziekte~~

= *"what has to be removed"*

Nieuwe criteria

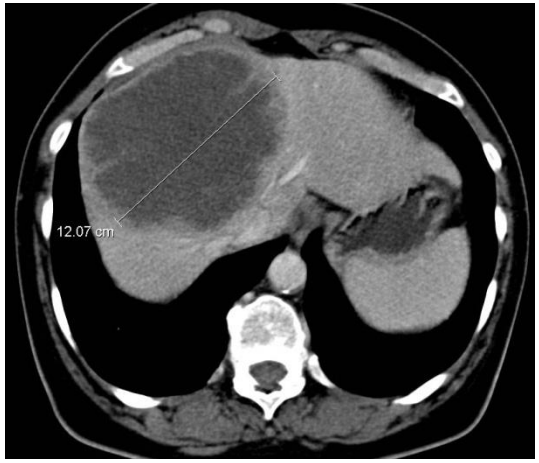
- R0 resectie
- "Future liver remnant" (FLR)

= *"what's left after resection"*

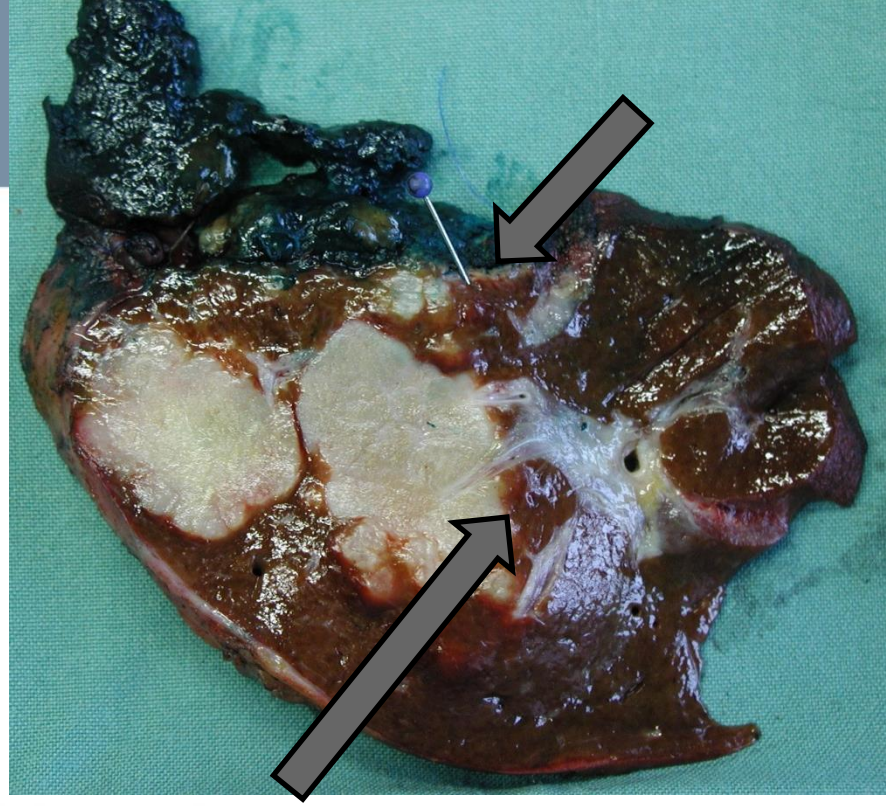
Reseceerbaarheid CRLM

Reseceerbaarheid: R0
Future liver remnant

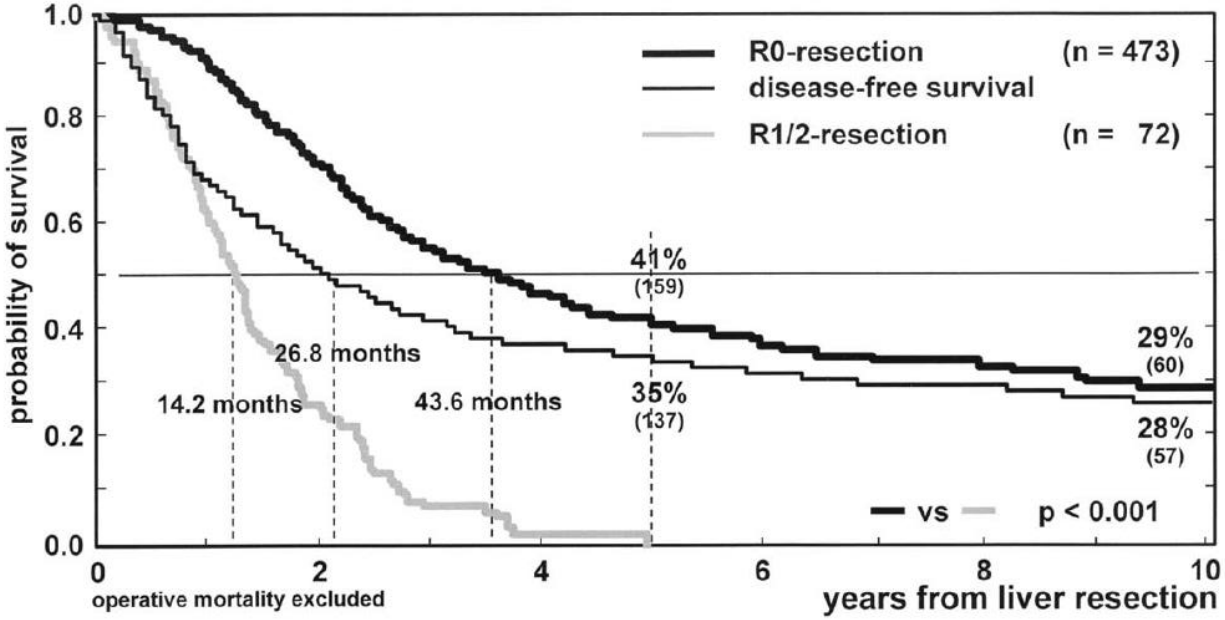
Geneesbaarheid: Tumor biologie
Tumor stadium



R0 resection vs. R1/R2 resection



R0 resection = essentieel !



Livermetsurvey 2010

Always 40% 5y survival after resection CRLM ?

Clinical risk score (CRS) *

** Memorial Sloan-Kettering Cancer Center*

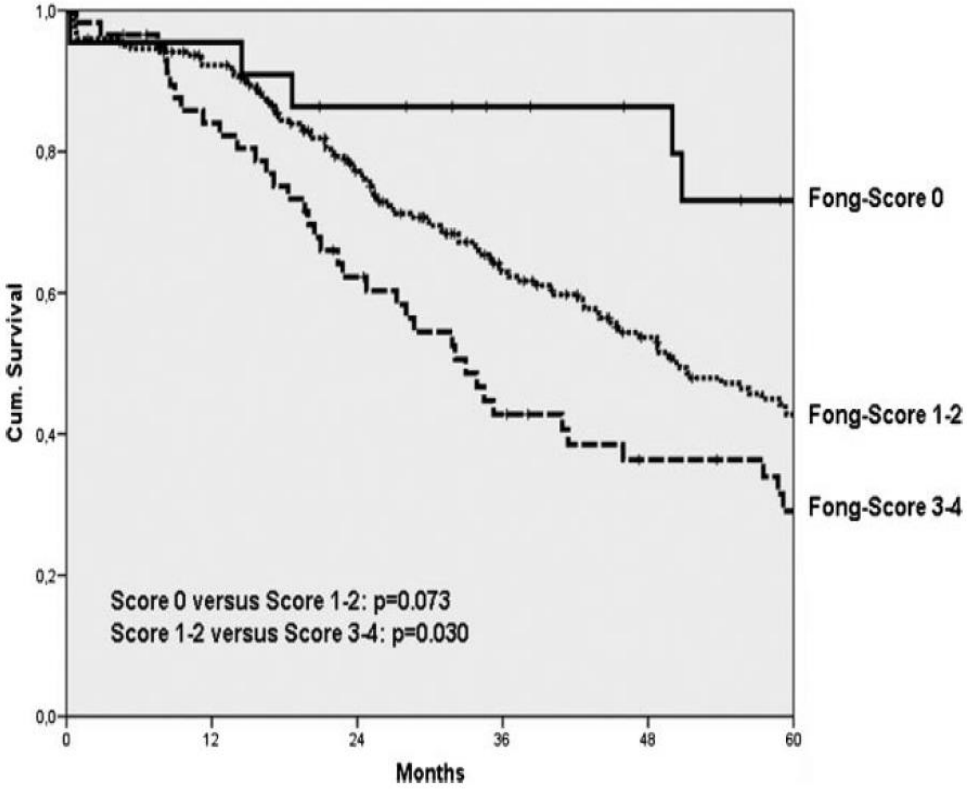
Fong, Ann Surg 1999

- Number of liver M >1
- Diameter M > 5cm
- Synchronous liver M
- LN status of primary tumor +
- CEA preop >200ng/ml

(scale 0 – 5)

Other scores:

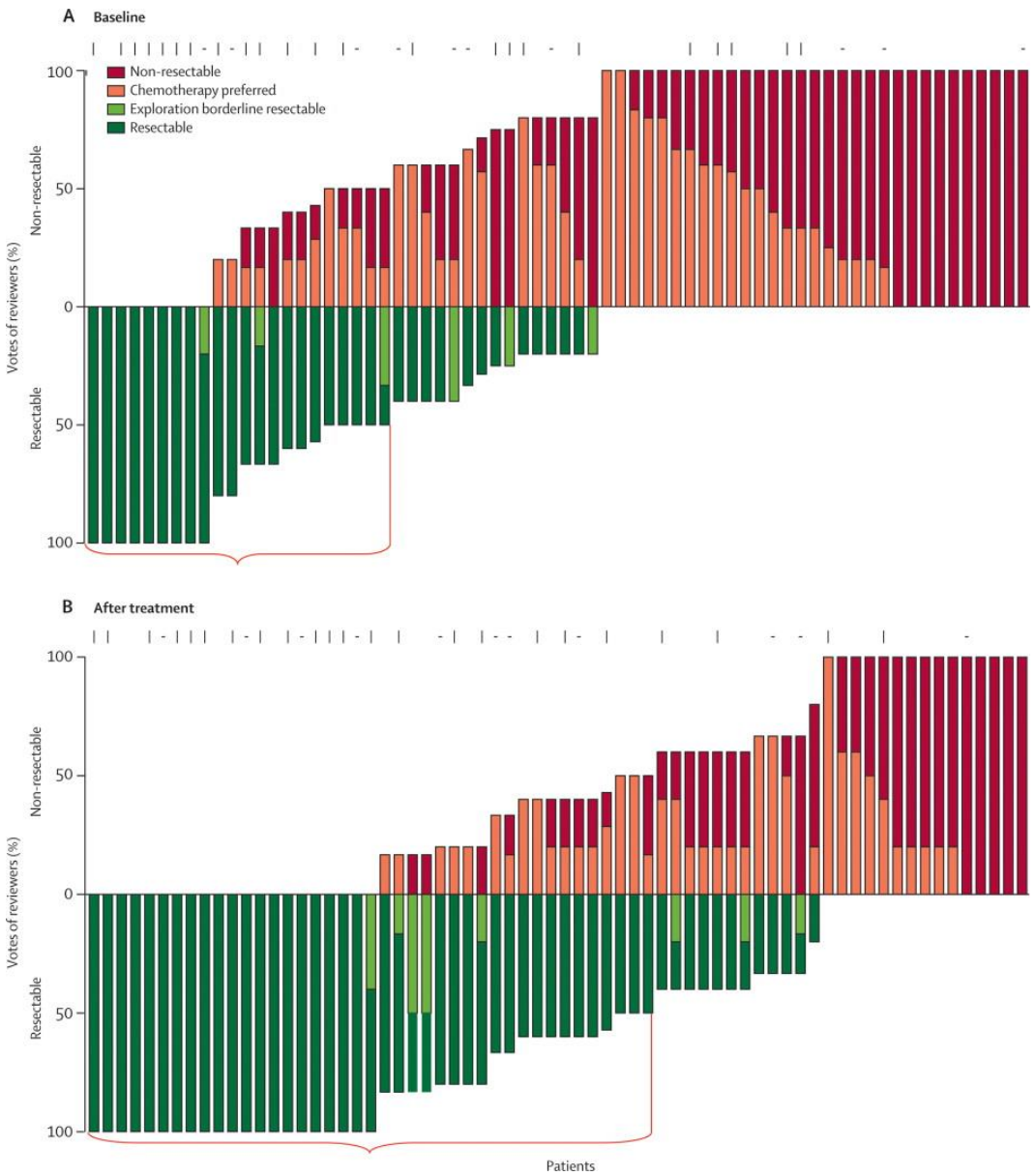
- Nordlinger score
- Iwatsuki score
- Basingstoke Index
- Mayo score system



Merkel, J Surg Oncol 2009

"Waterfall plot" van reseceerbaarheid

CELIM study 2010



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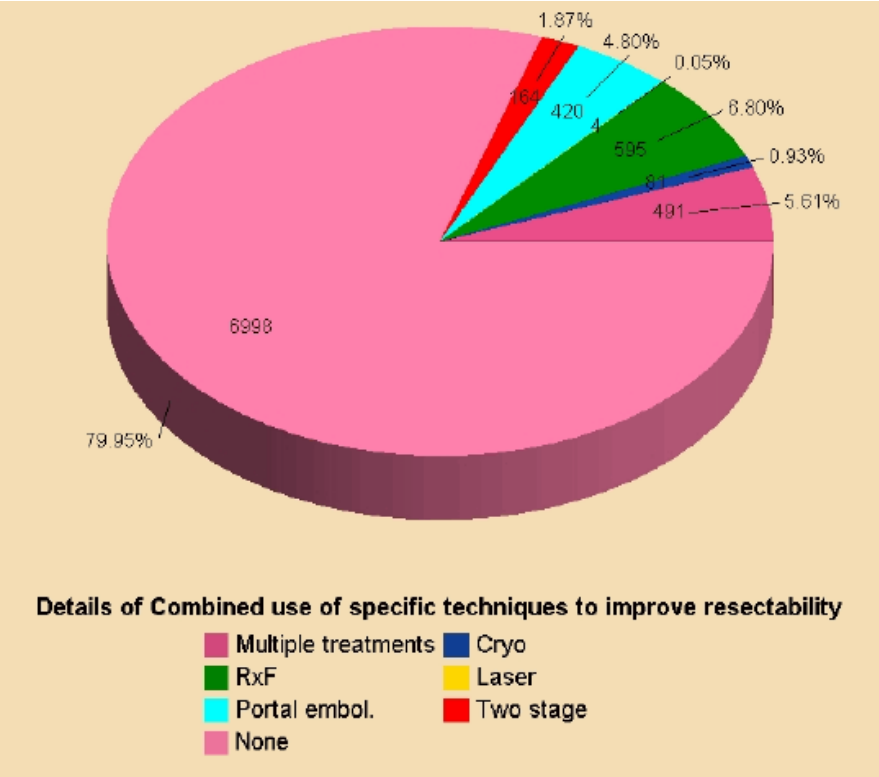
Potentieel reseceerbare CRLM: "how to get R0-resection and enough FLR ?"



Livermetsurvey, 2010

Bewaring zoveel mogelijk leverparenchym:

1. Neo-adiuvante chemotherapie
2. Radiofrequentie ablatie (RFA)
3. Kleinere resecties waar mogelijk

Vergroten "future liver remnant" (FLR):

4. Vena Porta embolisatie
5. "Two stage" hepatectomie

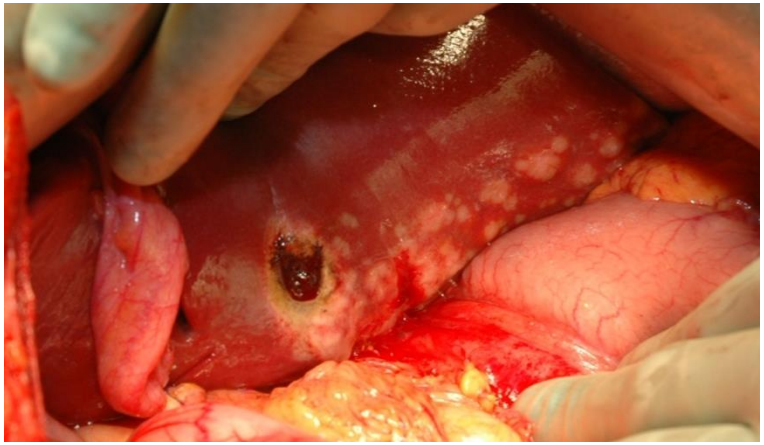
Bewaring excellente vascularisatie van FLR

6. Vascular reconstruction

1. Neo-adiuvante chemotherapie voor CRLM

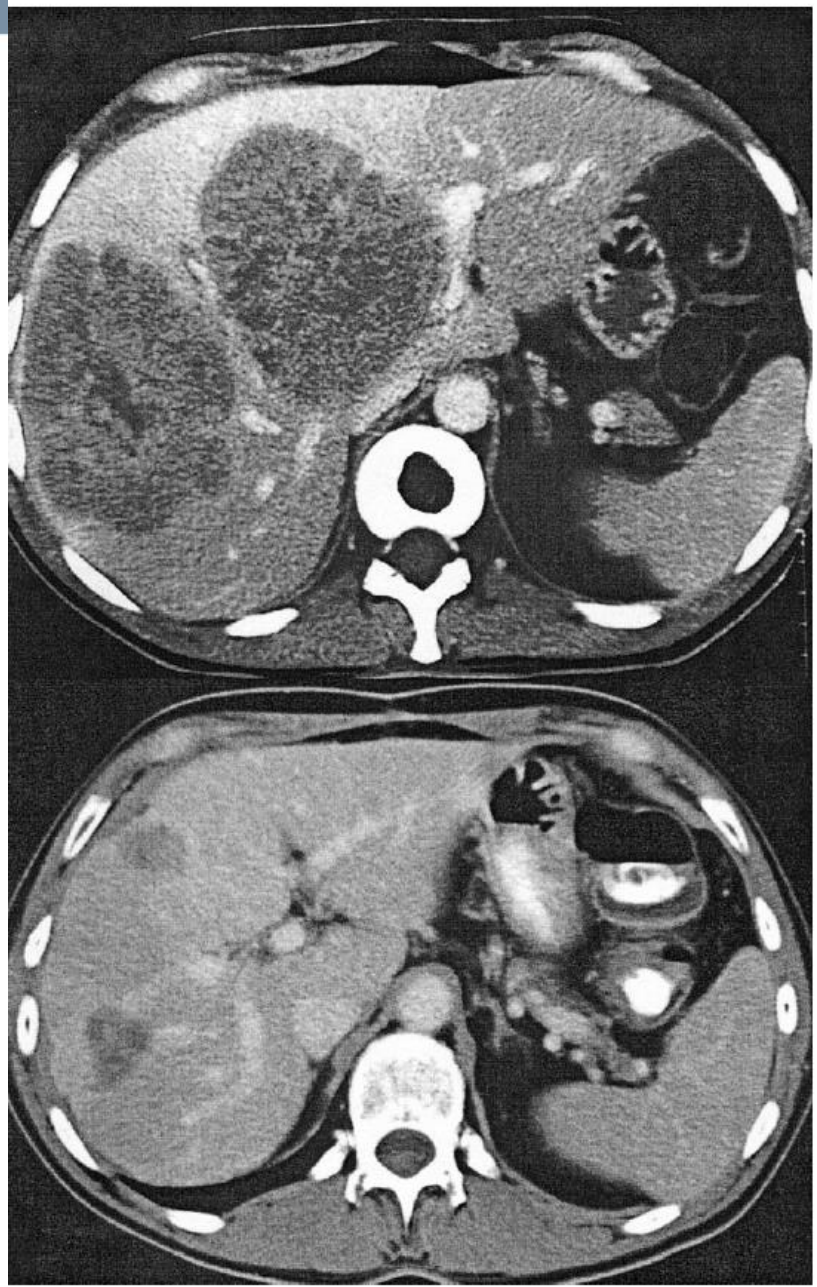
Potentiele benefits

- Tumor “downsizing”
- Eliminatie micrometastasen
- Testen van “chemoresponsiveness”

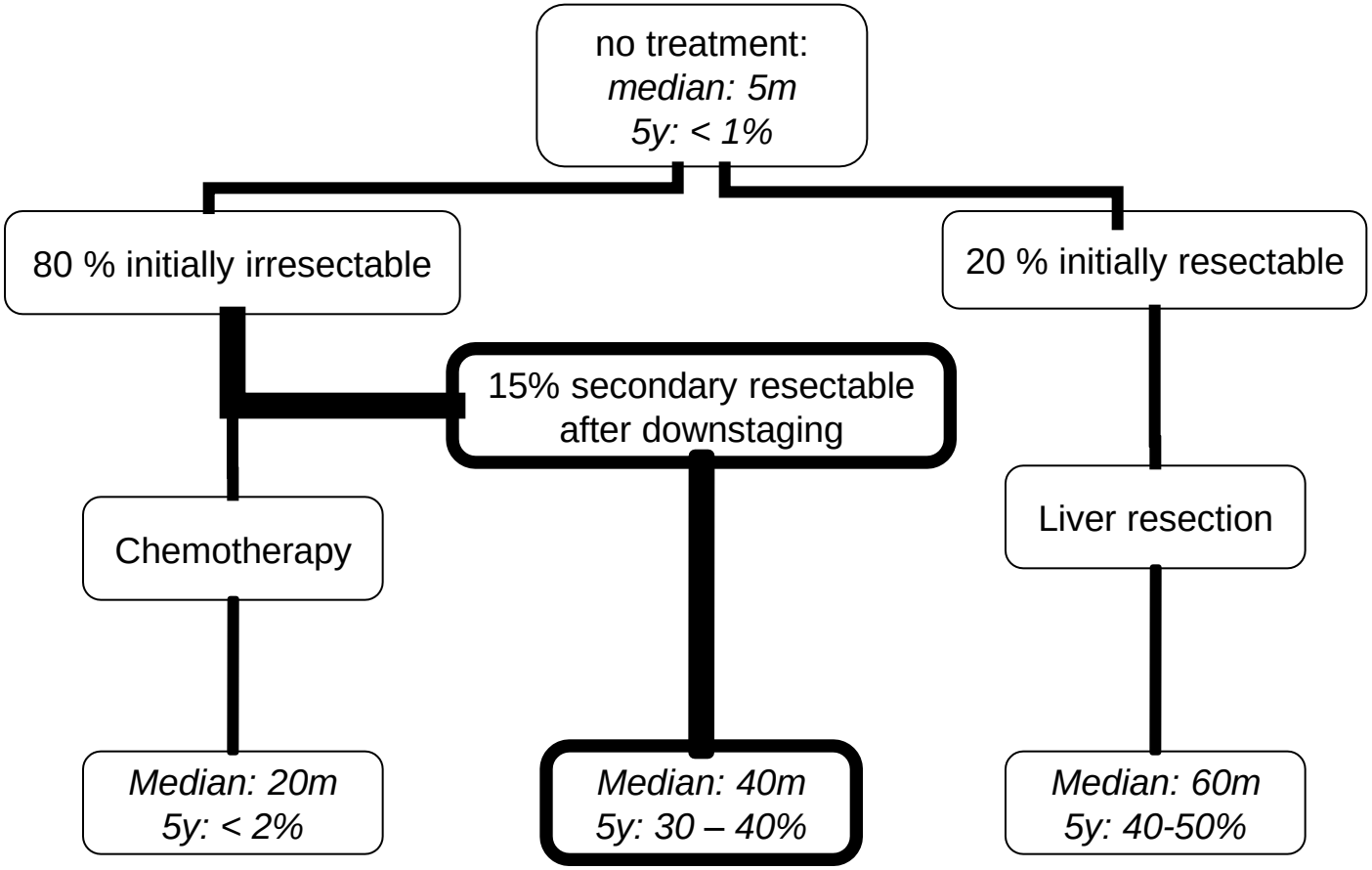


Potentiele nadelen

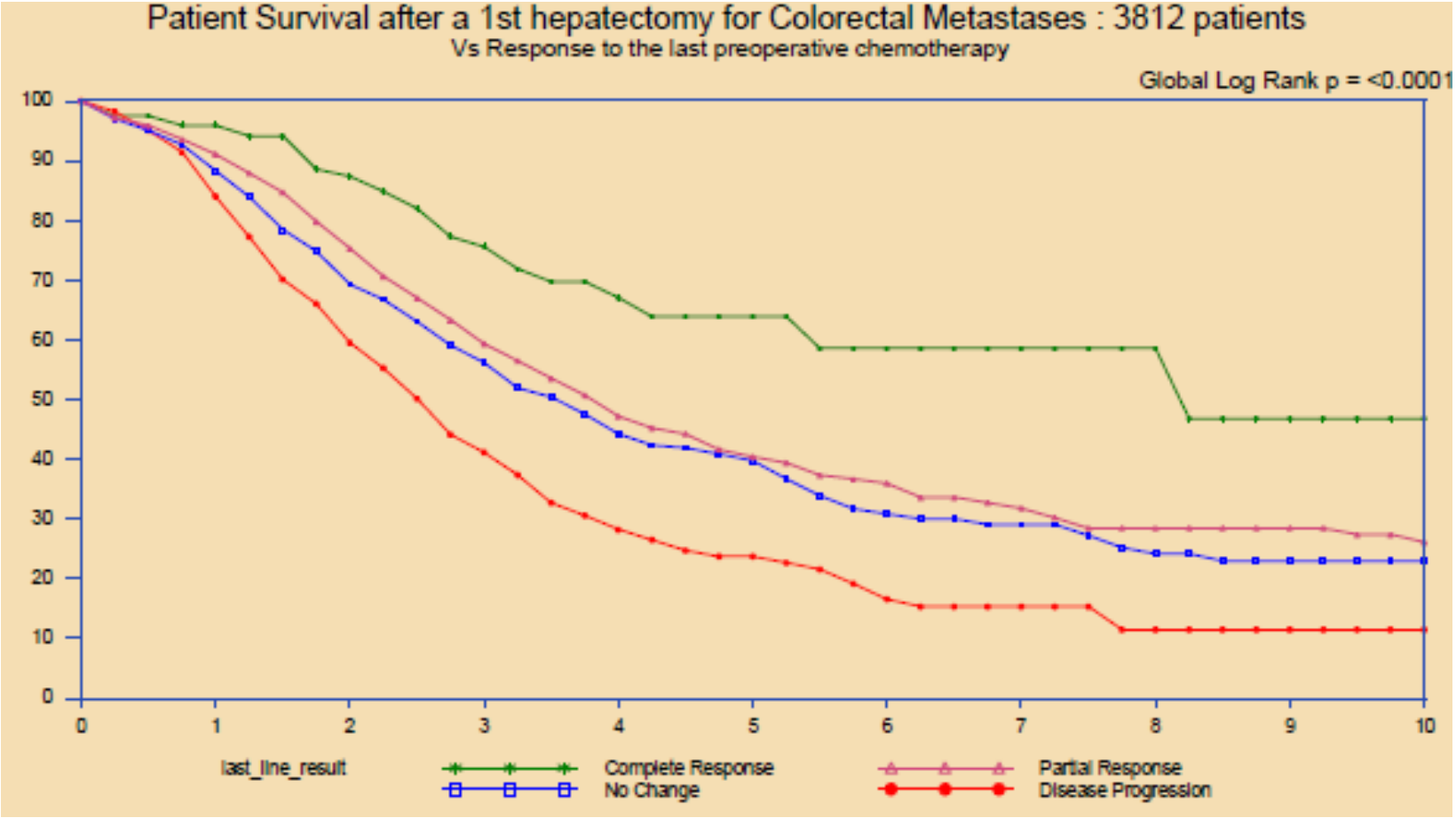
- Leverbeschadiging en gestoorde regeneratie
- Complete response (= “vanishing metastases”)



Downsizing with neoadjuvant chemotherapy



Test of chemoresponsiveness:
Is tumor progressie na CT een exclusie criterium voor resectie ?



Livermetsurvey, 2010

"Vanishing" metastasen na chemotherapie

- Complete radiologische respons na CT:

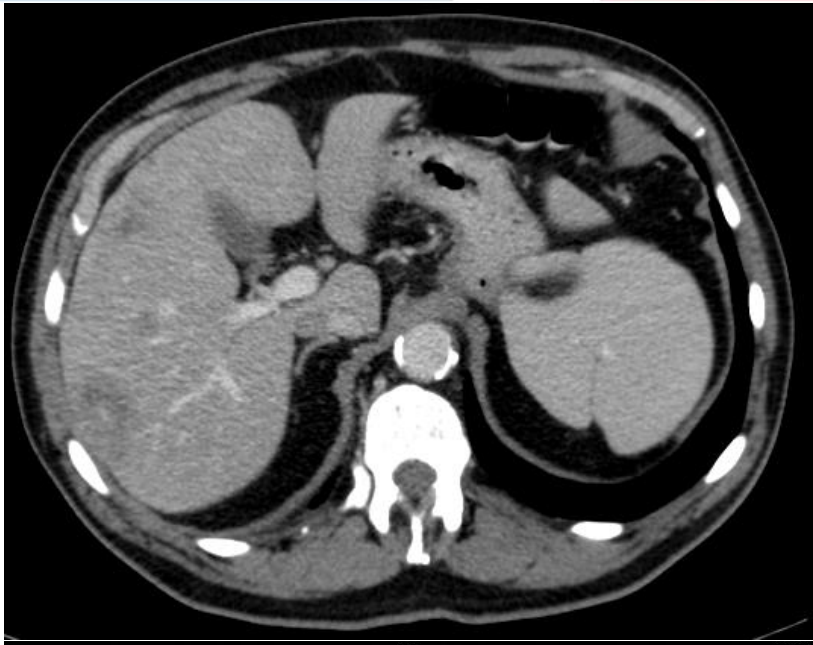
  → toch nog 93% actieve tumorale cellen bij pathologie

  → **<u>resectie indicatie blijft !</u>**

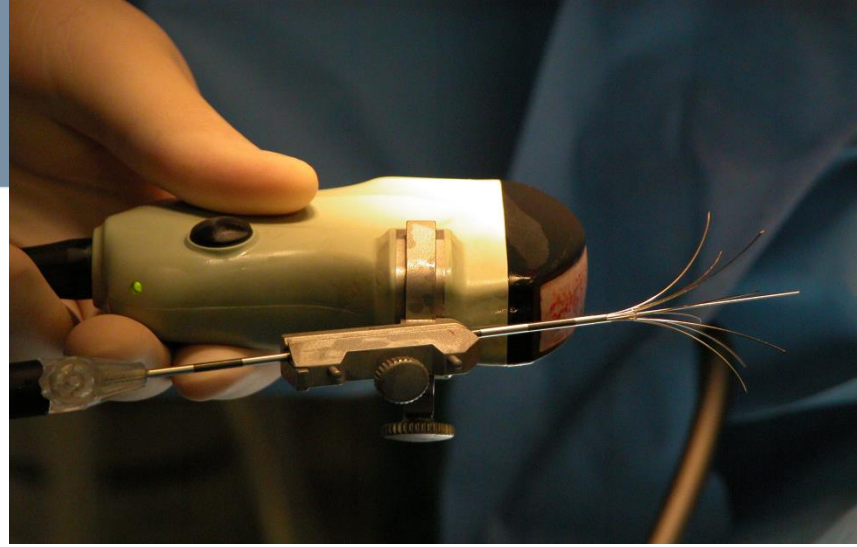
- Maar .... Resectie van deze “onzichtbare” metastasen”

  = technisch onmogelijk

→ Intermittente evaluaties tijdens CT en op tijd chirurgie !



2. RFA: combination with resection



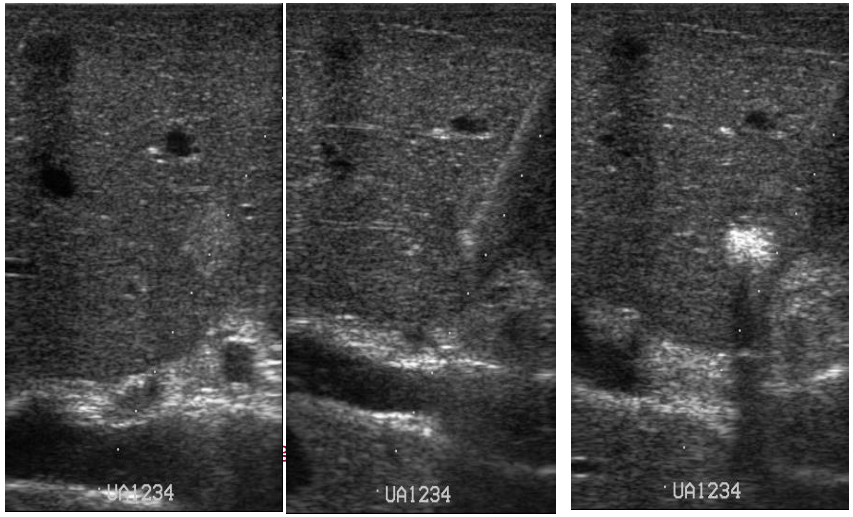
Normaal leverweefsel → FLR ≥ 30 %

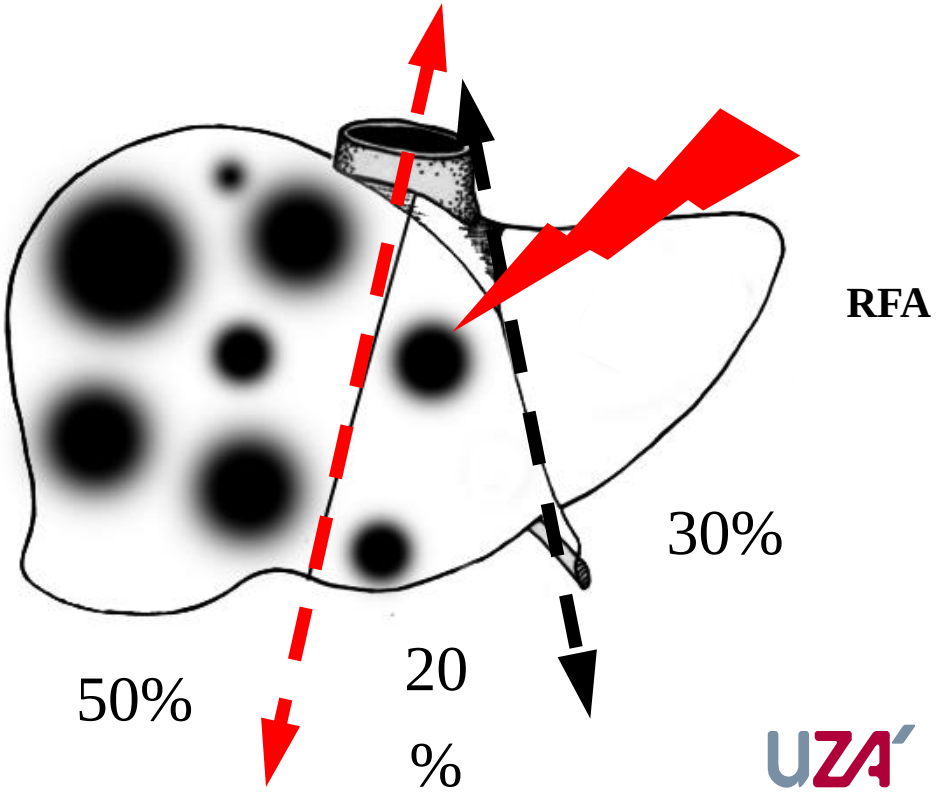
→ **extended right hepatectomy**

Gecompromitteerd liver → FLR > 40 %

→ **right hepatectomy**

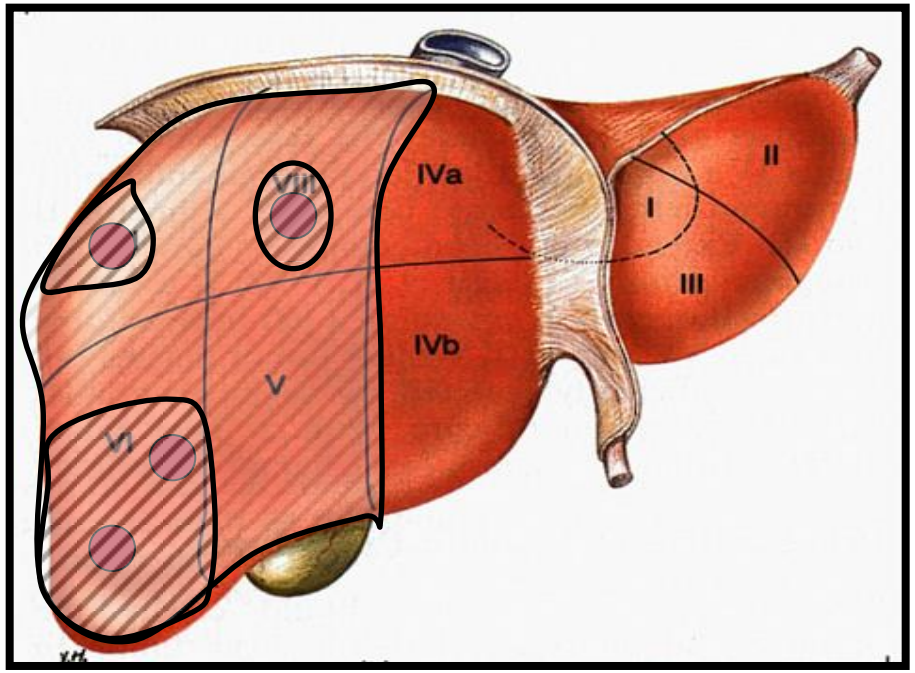
+ RFA in segment 4

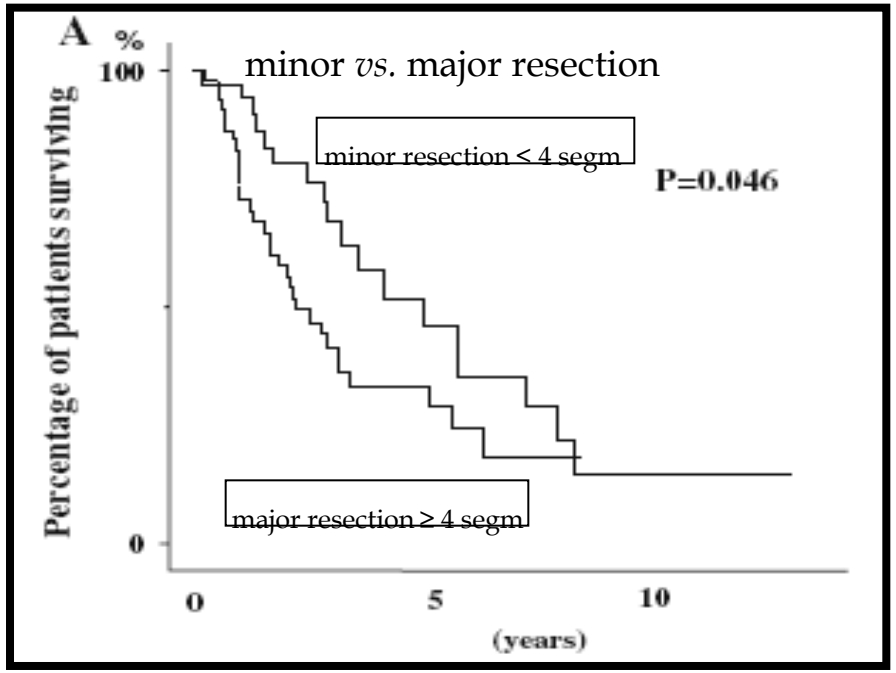




3. Kleinere leverresecties – maximale bewaring gezond leverparenchym

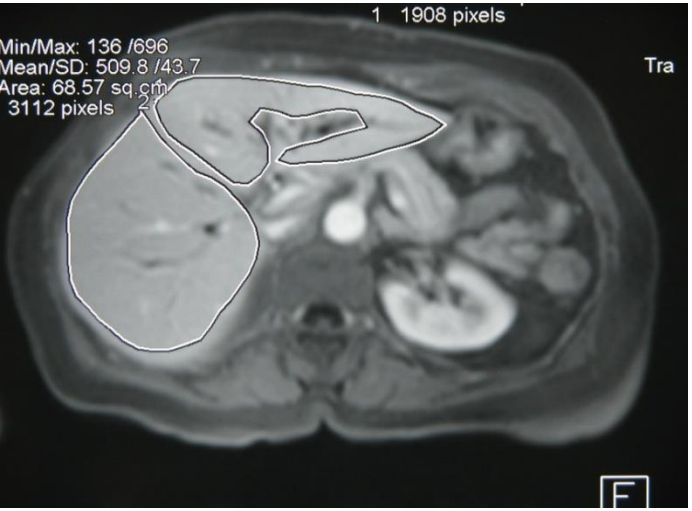
Overall survival in resection for ≥ 4 CRCM:

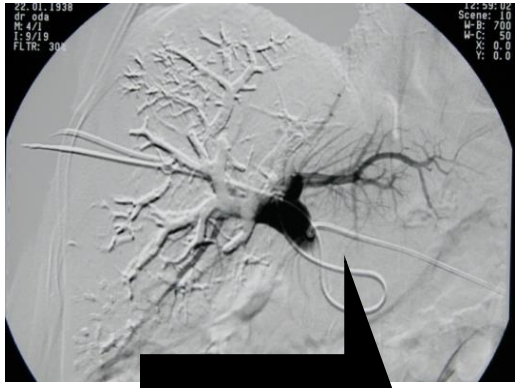


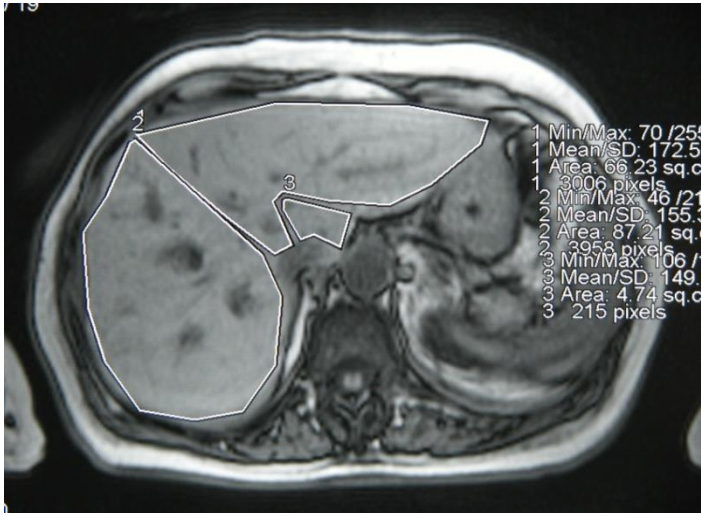


4. Vena Porta Embolisatie (PVE)

Doel: hypertrofie van de te bewaren leverrest



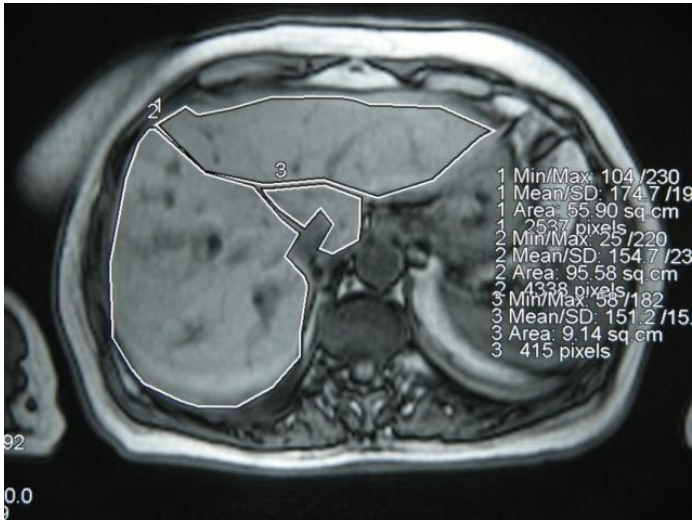




R: 71% L: 28%

4-6 wk

R: 62% L: 36%



5. "Two stage" hepatectomie

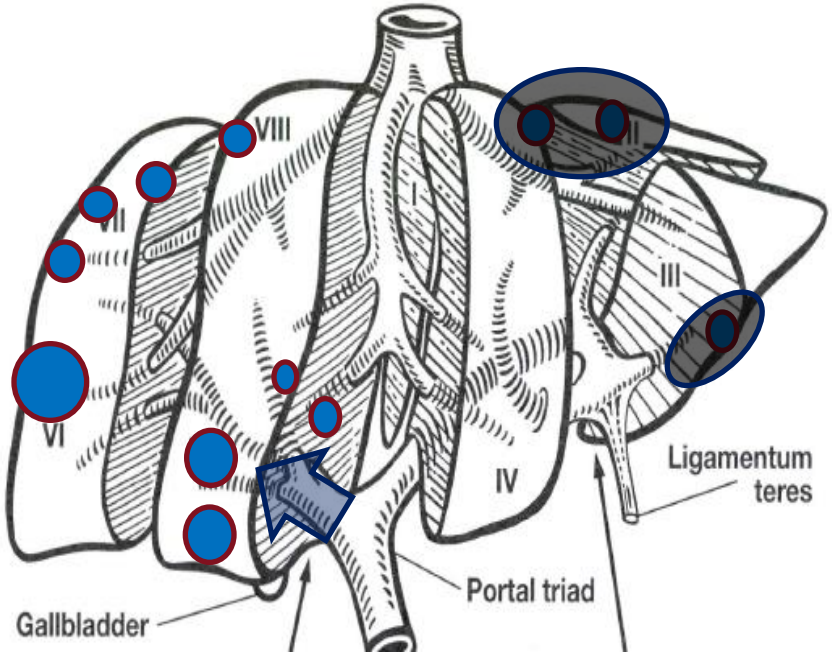
1st stage

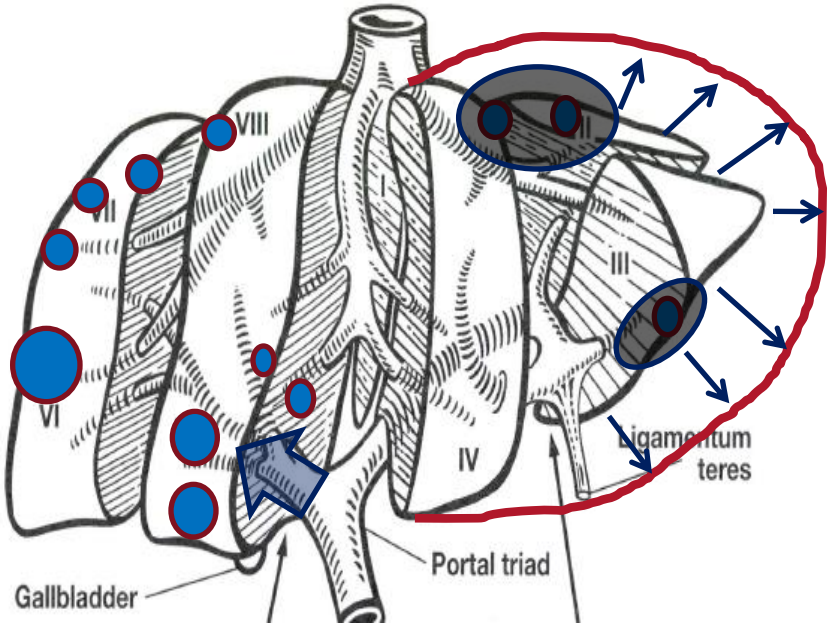
- Verwijdering alle CRLM in de te bewaren leverrest
- PVE van de contrateral hemilever

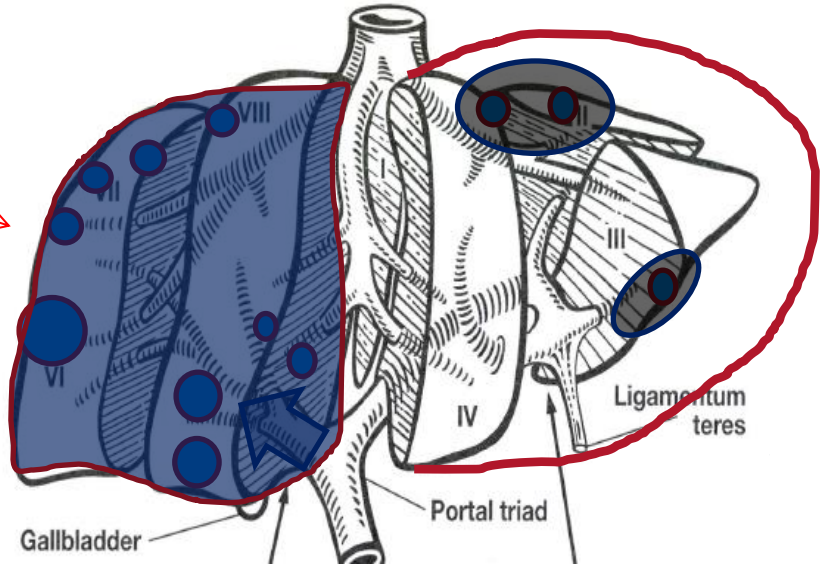
Hypertrophie van de ipsilaterale hemilever

2nd stage (na 6-8wk)

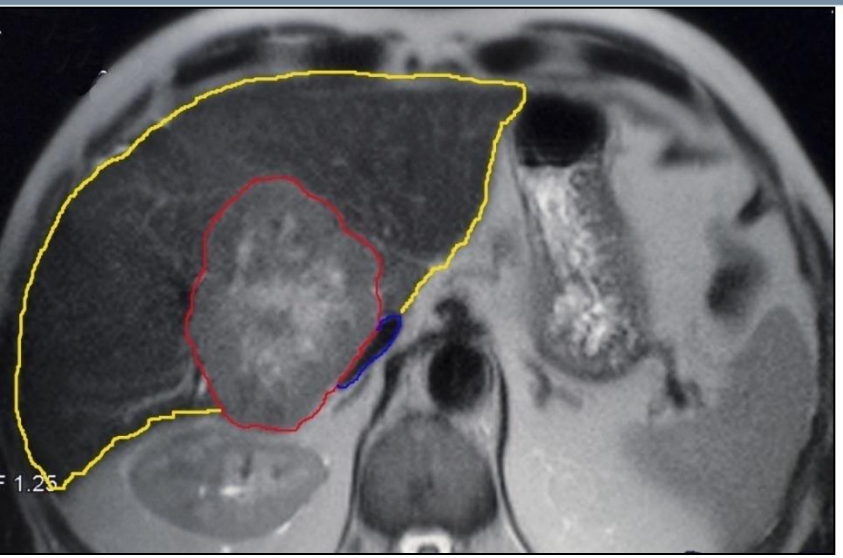
- Contralaterale hemihepatectomie

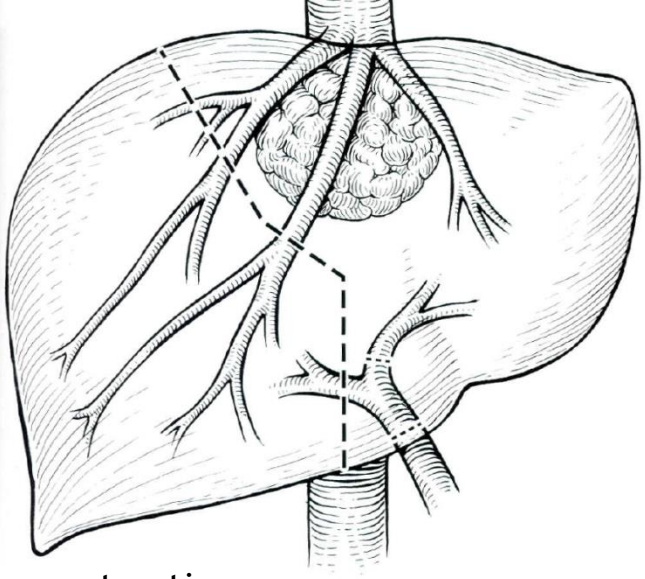






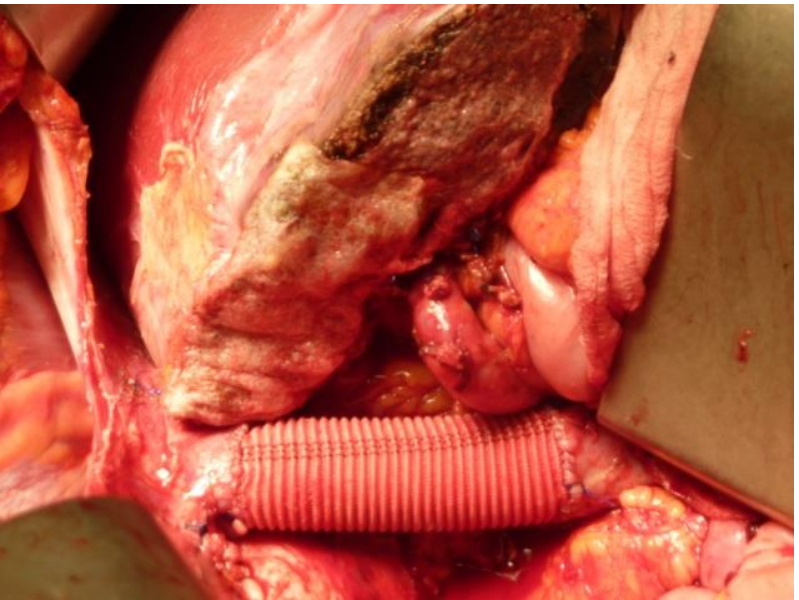
6, Vasculaire reconstructies bij invasie van grote bloedvaten



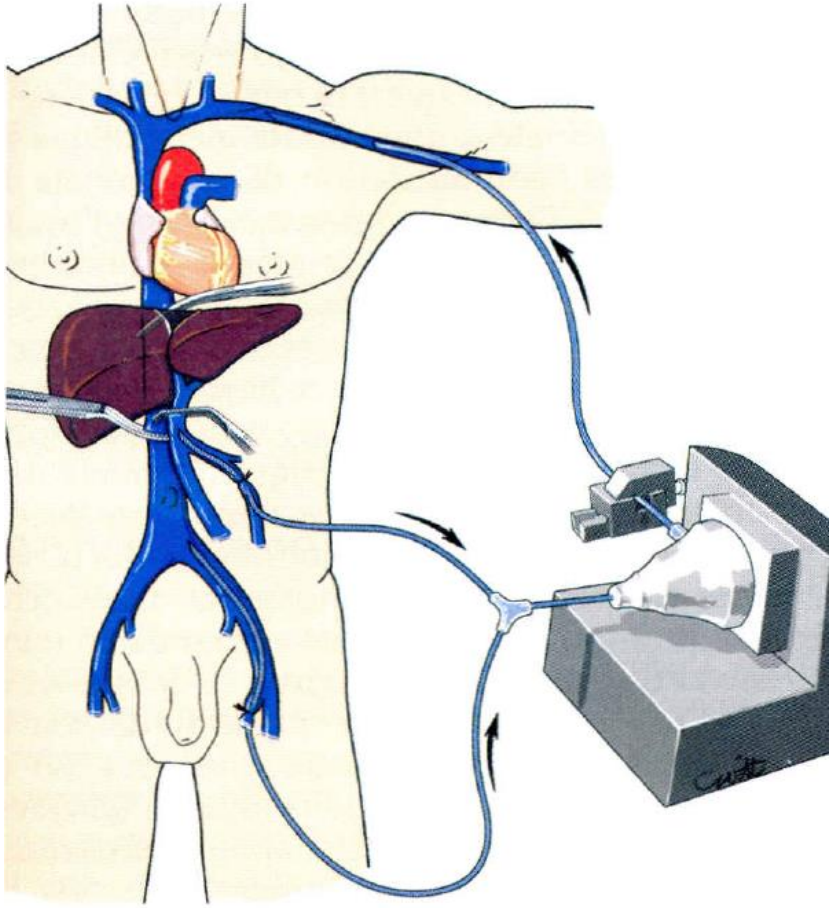


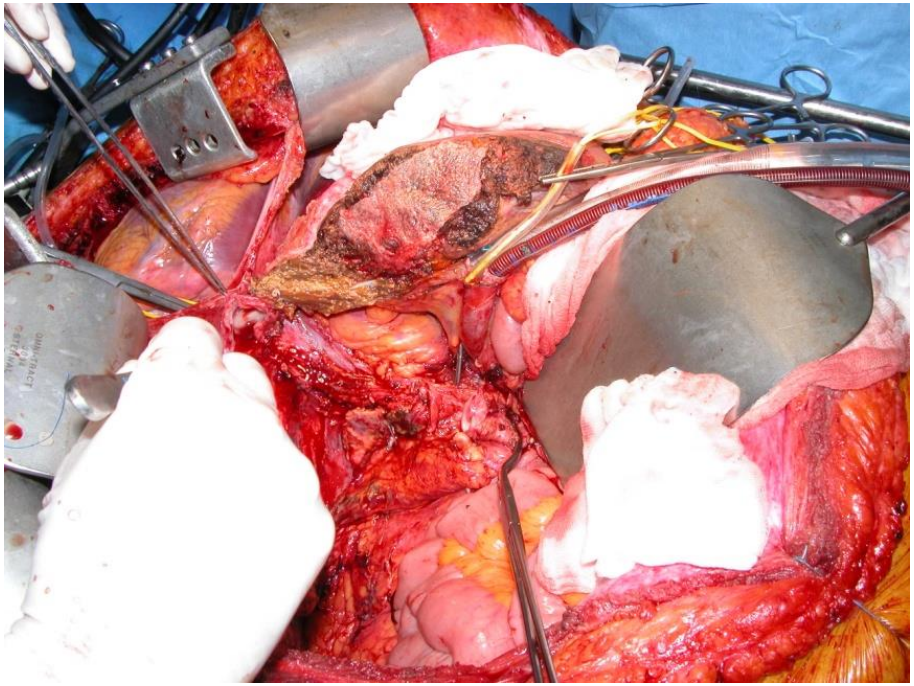
Vascular reconstruction:

- Retrohepatic vena cava
  - Hepatic vein
  - Portal vein



Temporary veno-porto-venous bypass
- implementatie van transplant technieken -





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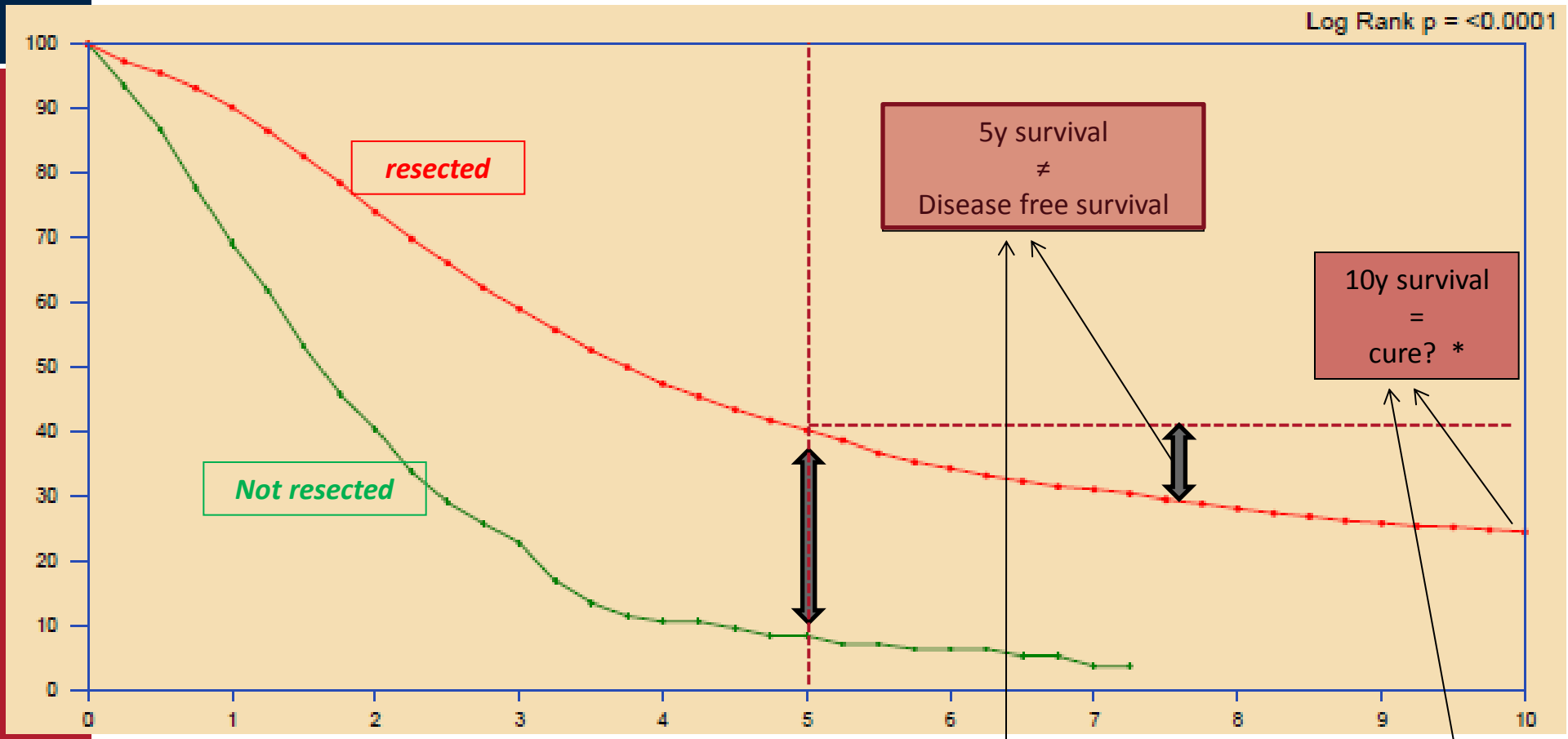
R0 resectie van CRLM = “genezing” CRLM ?

Livermetsurvey, June 2010

Patient survival



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Resected	90%	74%	59%	47%	40%	34%	31%	28%	26%	24%
Not res.	69%	40%	23%	11%	8%	6%	4%			

Take home messages

Colorectale levermetastasen : geen hopeloze situatie !!

Integendeel : indien mogelijk, biedt RO chirurgie de (bijna) enigste op genezing

Levermetastasen chirurgie :

- Vraagt voorbereiding en timing via MDO
- Gans arsenaal ter beschikking om chirurgie mogelijk te maken
- "sky is the limit" indien biologisch zinvol geacht (MDO)
- implementatie van technieken van levertransplantatie

Indien RO resectie : 5 j overleving 10-15 % → (minstens) 40 %

Liver transplantation for CRM ? → TRANSMET

Chemotherapy and Liver Transplantation versus Chemotherapy alone in the treatment of definitively unresectable liver metastases from colorectal cancer (MCR): a prospective multicentric randomized trial

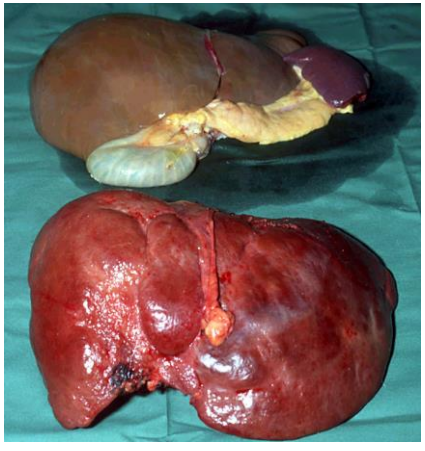
= TRANSMET (a French – Belgian study)

To validate LT as a recognized treatment option in very well selected patients suffering from confirmed unresectable LMCR

To base the selection process not only on a surgical consideration but on a multidisciplinary decision involving medical oncologists, radiologists, pathologists and surgeons

To reach a 5-year survival of at least 50% by restricting the candidates to patients younger than 60 yrs, with metastases responding to ≤ 2 lines of chemotherapy while remaining unresectable, with CEA / CA19-9 levels < 100 ng/ml and a previous high standard carcinological resection of the primary and by combining LT to perioperative chemotherapy

→ n = 2 x 40 pts (2015-2018)



Das Große Fressen – P.J. Orth