Disclosure belangen Arjan Diepstra

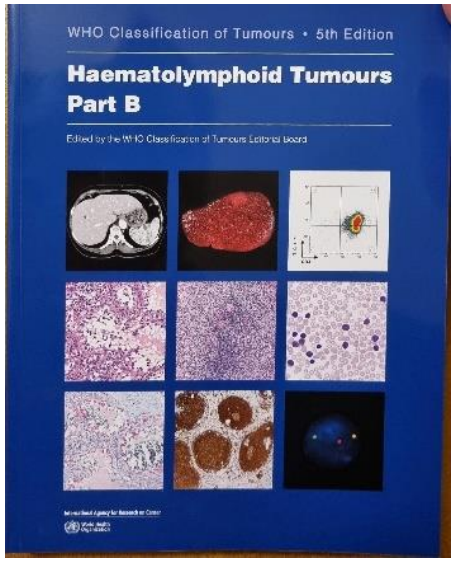
(potentiële) belangenverstrengeling	Geen
Voor bijeenkomst mogelijk relevante relaties met bedrijven	Bedrijfsnamen
• Sponsoring of onderzoeksgeld • Honorarium of andere (financiële) vergoeding • Aandeelhouder • Andere relatie, namelijk …	• • • •

Histologie van rijpe lymfatische B-cel maligniteiten - het beenmergbiopt -

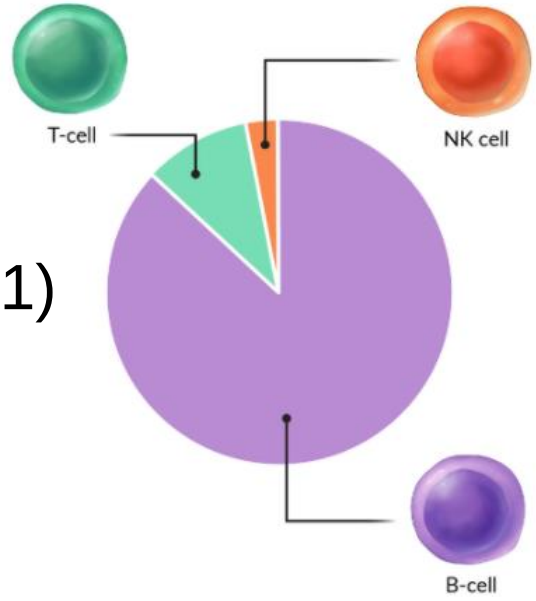
Arjan Diepstra
Pathologie, Groningen

Wenckebach basiscursus Cytologie en Histologie van bloed en beenmerg, Groningen 2024

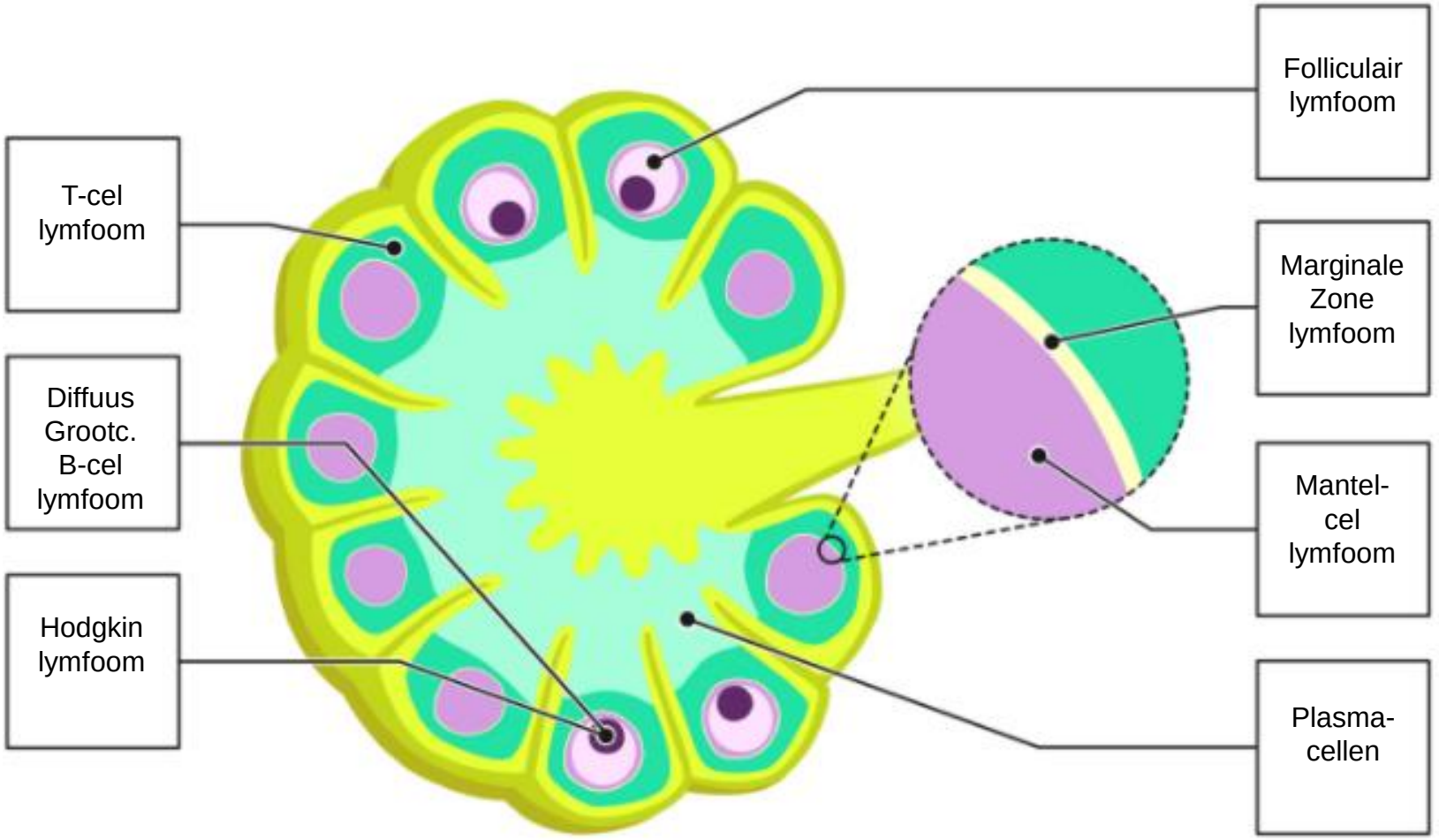
Soorten lymfatische maligniteiten



- > 50 verschillende soorten
- Histologie is de gouden standaard
- Indeling gebaseerd op:
  - cel van origine: B-cel vs. T-cel
  - B:
    - gelijkenis tov normale counterpart
    - groeiwijze
    - morfologie (groot/klein)
    - specifieke translocaties
    - virus (EBV, HHV8, HTLV-1)
    - klinische presentatie

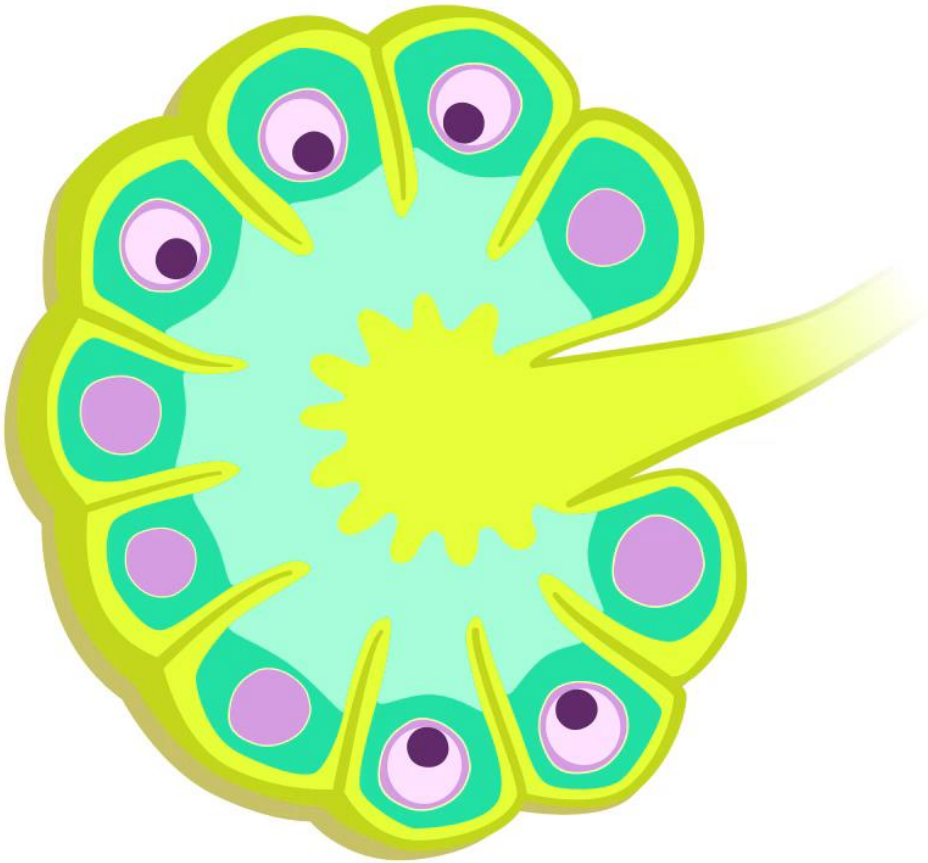


Normale counterparts in de lymfklier



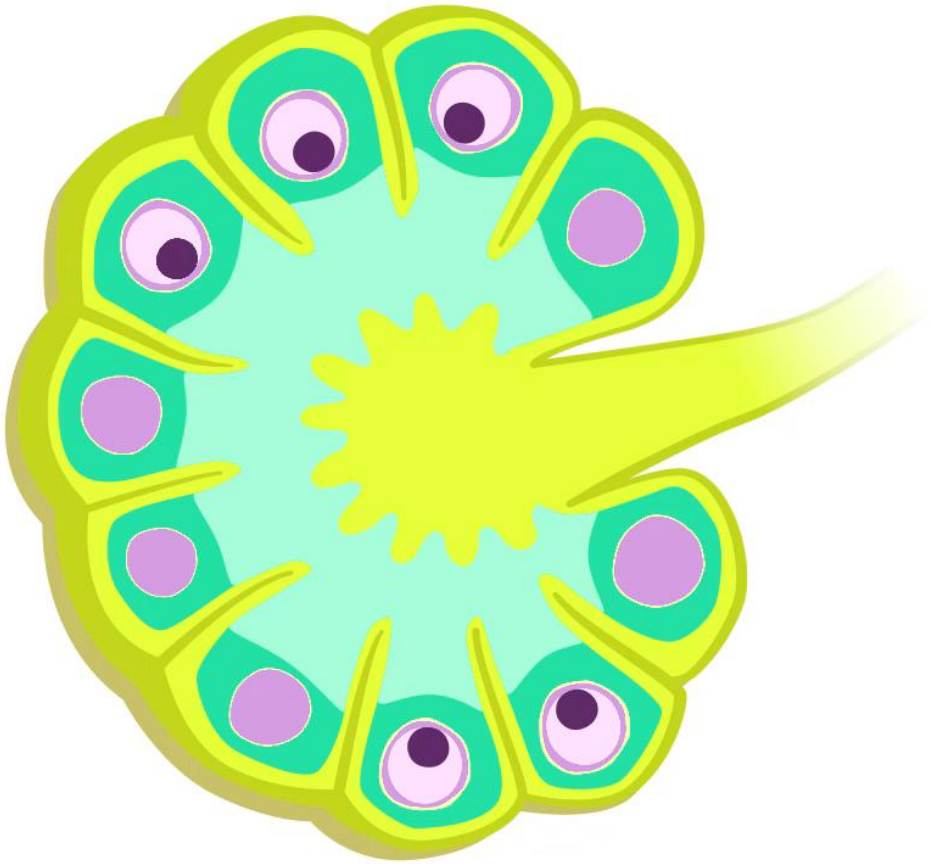
- NB: Ca. 50% extranodaal (GE, huid, long, beenmerg etc)

Groeiwijze



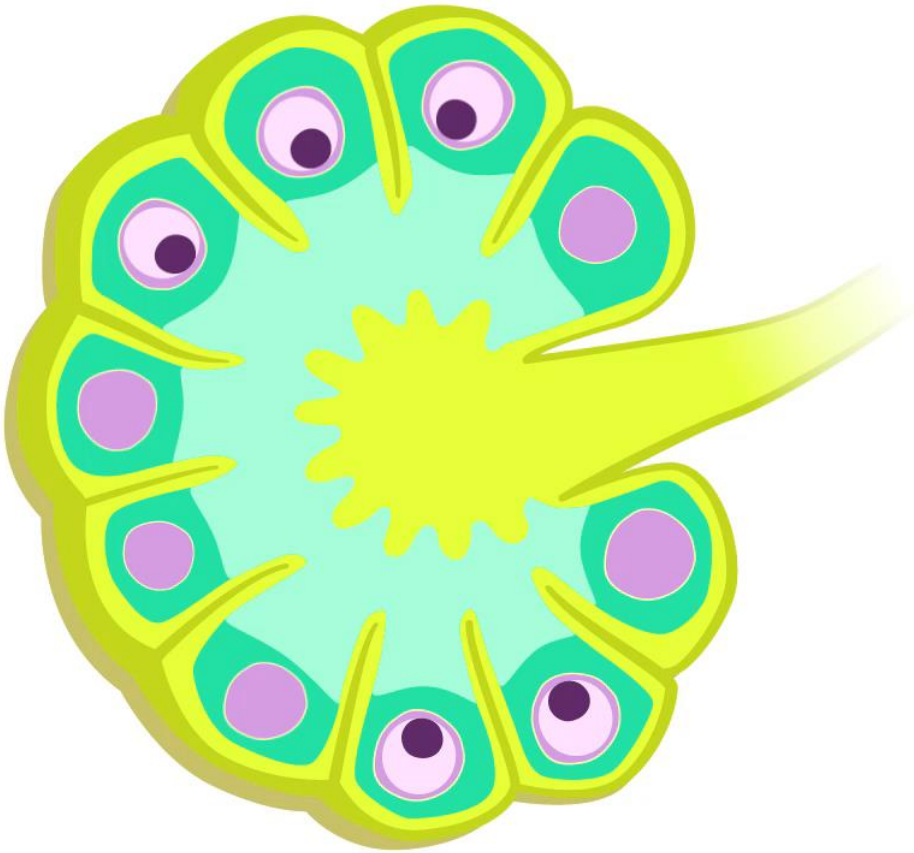
Folliculair lymfoom

Groeiwijze



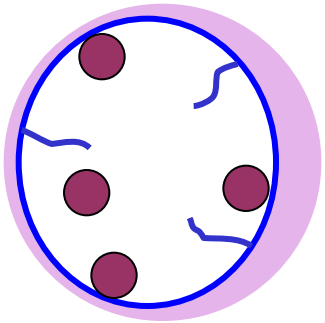
Marginale zone lymfoom

Groeiwijze



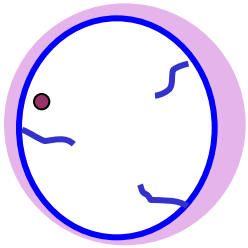
Hodgkin lymfoom

Morfologie – in detail



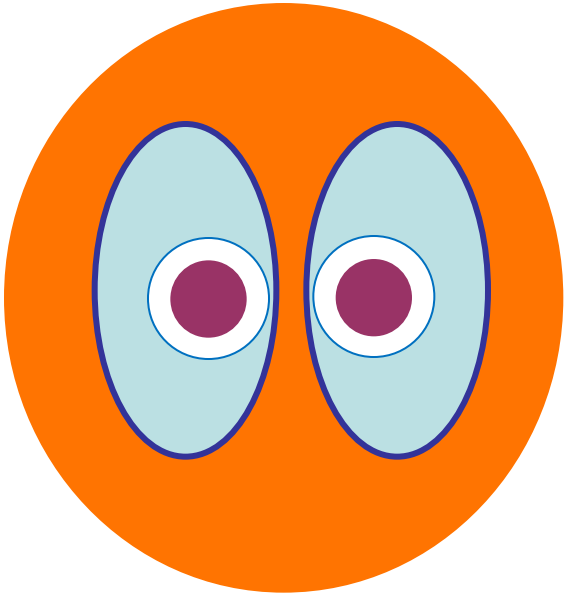
Centroblast

DLBCL



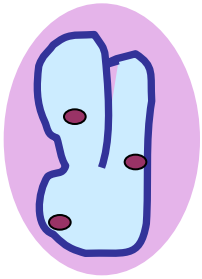
“Middelgrote blast”

Burkitt, LBL



Reed-Sternberg cel

Hodgkin

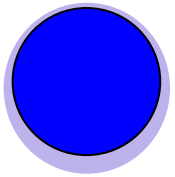


Centrocyt

Foll. lymfoom

grof chromatine

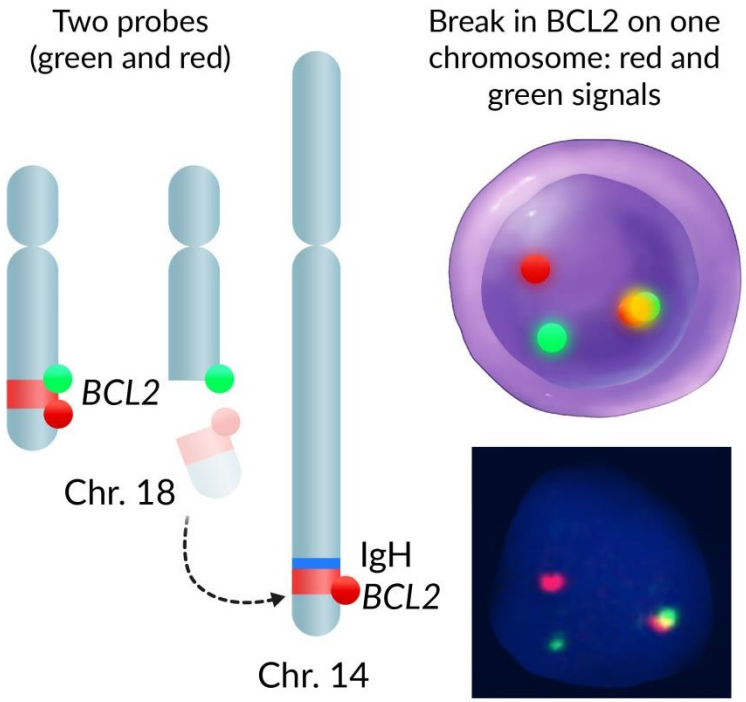
kleincellig lymfocytair/ CLL



Normale B cel

Translocaties

- Burkitt lymfoom	- cMYC-IgH	t(8;14)
- Mantelcellymfoom	- Cycline D1-IgH	t(11;14)
- Folliculair lymfoom	- BCL2-IgH	t(18;14)
- “Double hit”	- cMYC + BCL2	



Indicaties beenmergbiopt

- diagnostisch
    - bij cytopenie, paraproteïne, grote milt
    - moeilijk/niet te bereiken lymfomen
    - sporadisch bij lastig te classificeren lymfomen

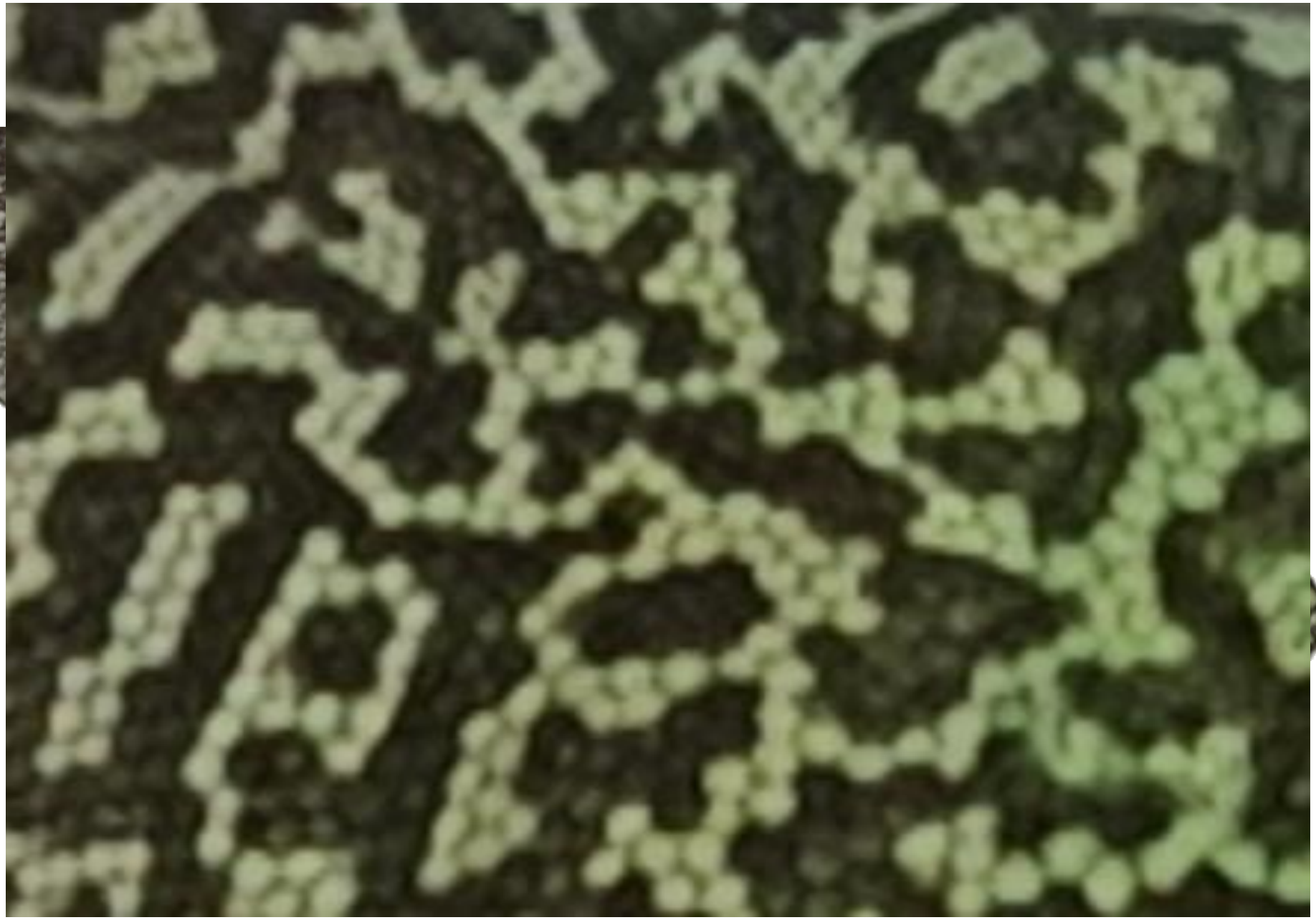
- stadiëring bekend lymfoom
    - Ann Arbor stadium IV
    - *kwaliteit en kwantiteit biopt van belang*

- follow-up / responsevaluatie na therapie
    - na (chemo-)therapie
    - na beenmergtransplantatie

Incidentie B-cel lymfomen in beenmerg bij diagnose

B-cel lymfoom type	% in beenmerg
Lymfoplasmacytair	~100%
Milt marginale zone	70%-100%
Kleincellig lymfocytair	85%
Mantel cel	55%-95%
Folliculair	50%-60%
Burkitt	35%-60%
Extranodaal marginale zone/ MALT	30%-45%
Diffuus grootcellig B-cel	15%-30%

Uit: Knowles' 2014

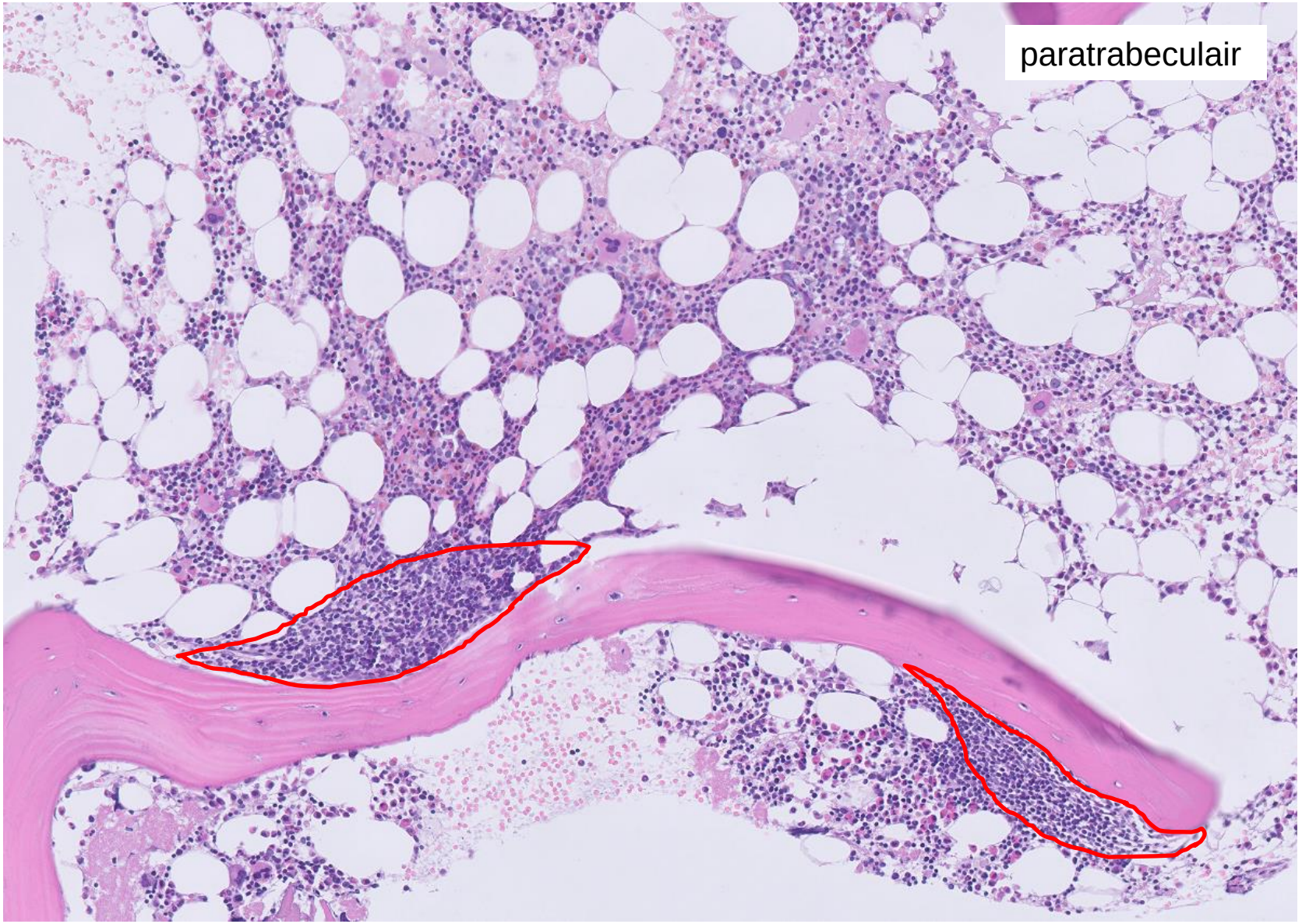


Beoordeling lymfoïde infiltraten

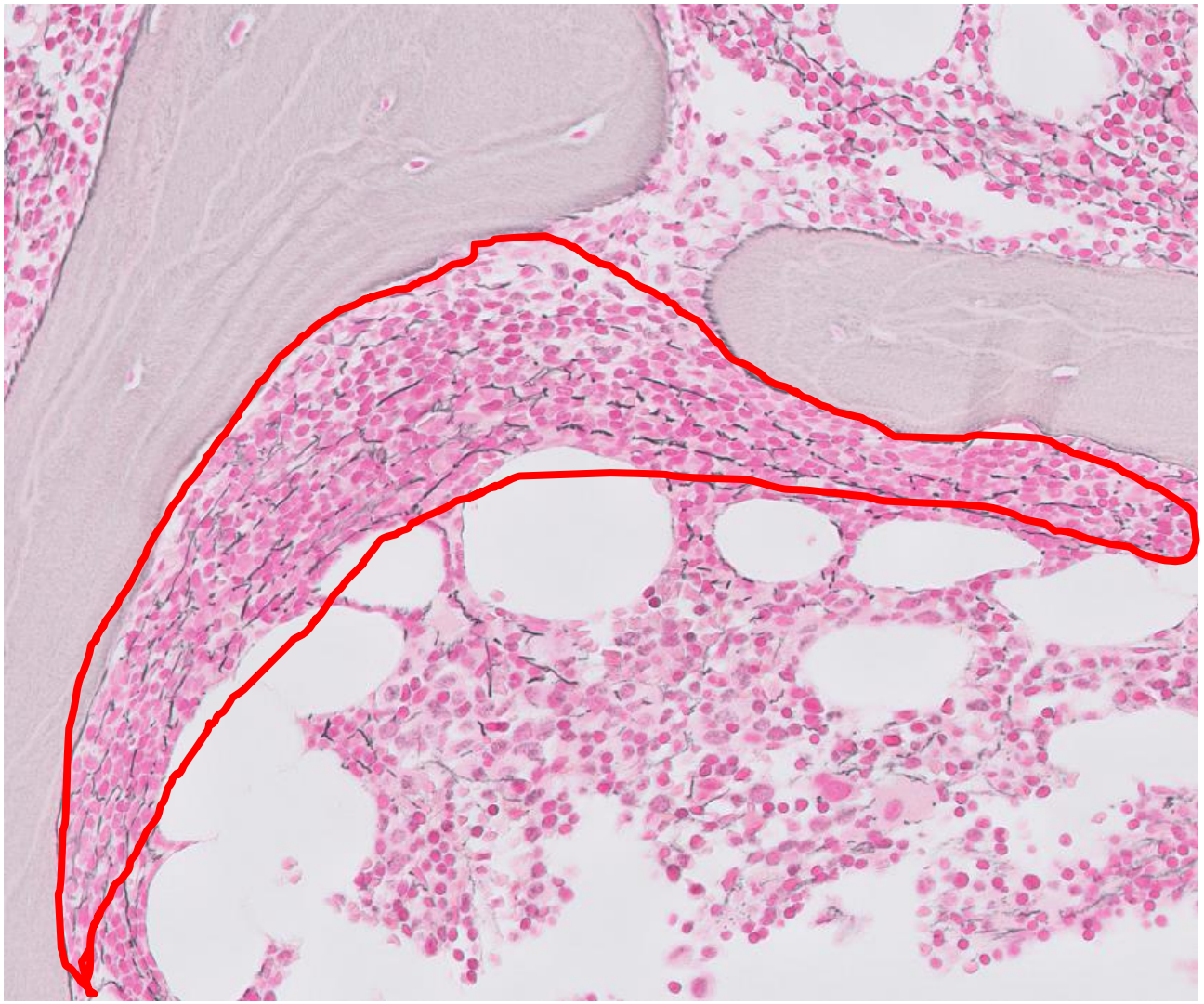
- Gehele biopt op lage vergroting
    - celrijkdom, ligging vetcellen, toegenomen “blauw”

- Distributie:
    - focaal paratrabeculair (langs botbalkjes)
    - focaal nodulair (centrale haardjes)
    - diffuus (verdringing vetmerg en hematopoiese)
    - interstitieel (vetmerg intact), +/- IHC
    - intravasculair/intrasinusoidaal, +/- IHC

Distributie



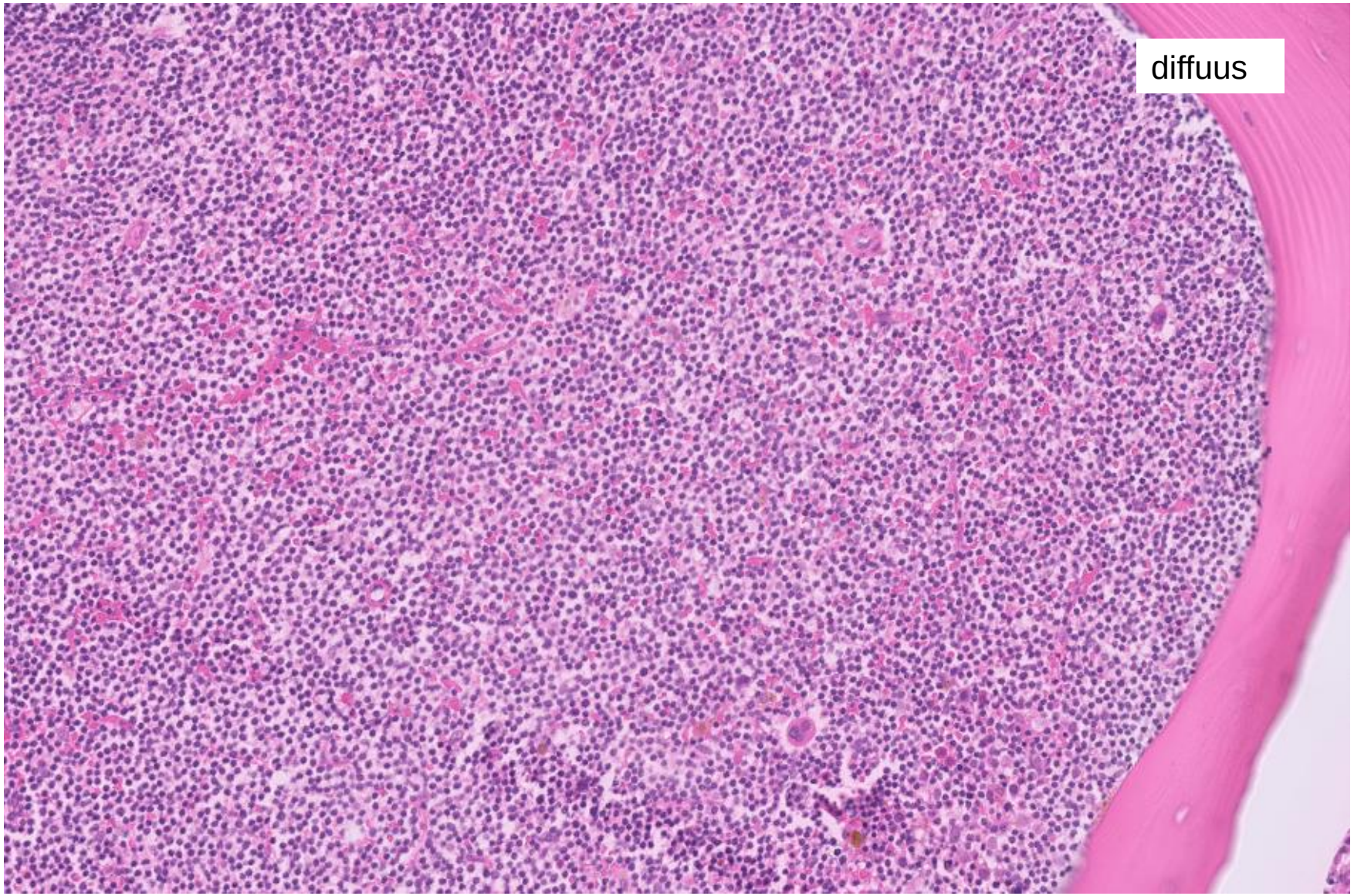
Paratrabeculair ~ Folliculair lymfoom



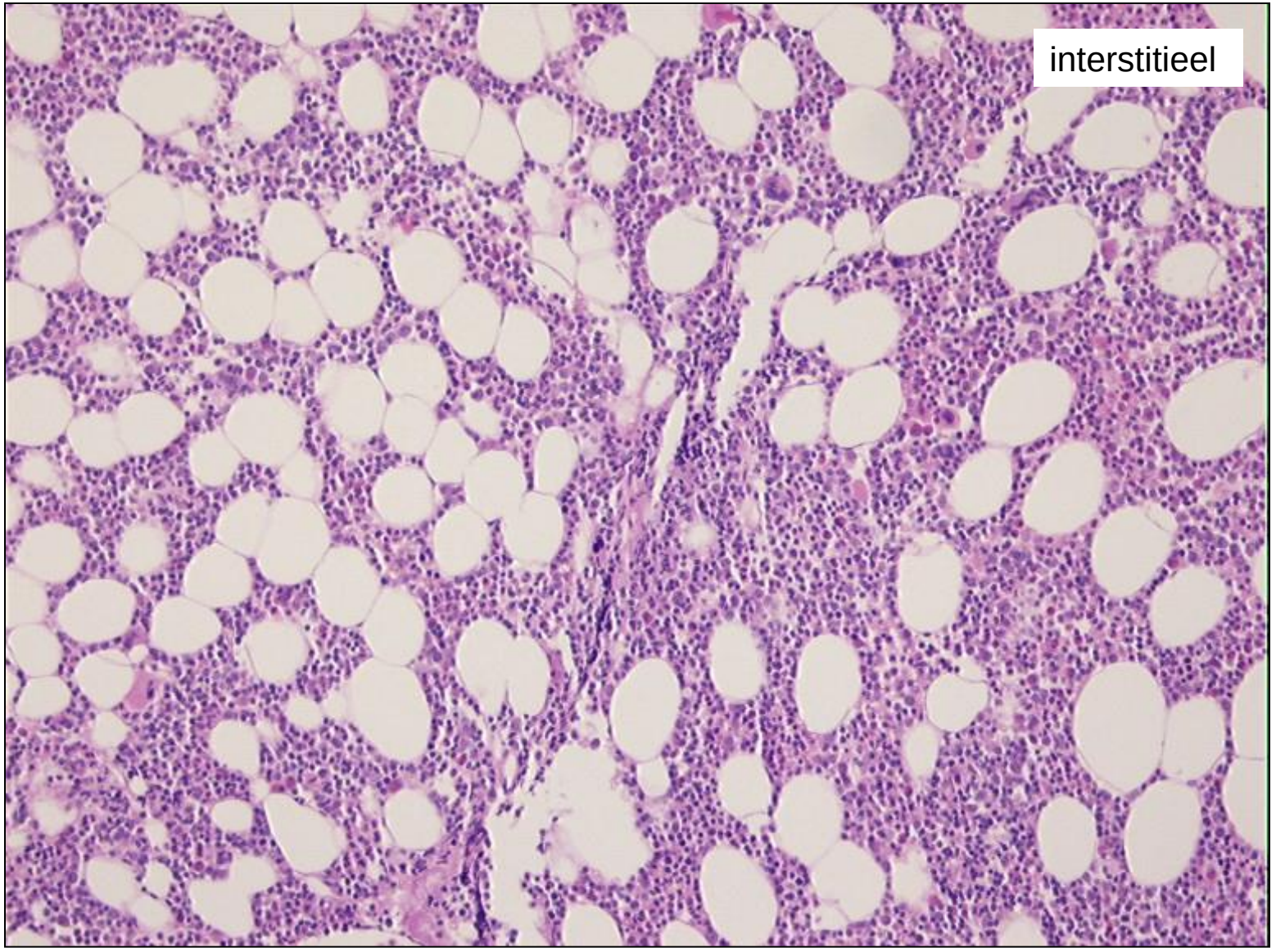
Reticuline

Distributie

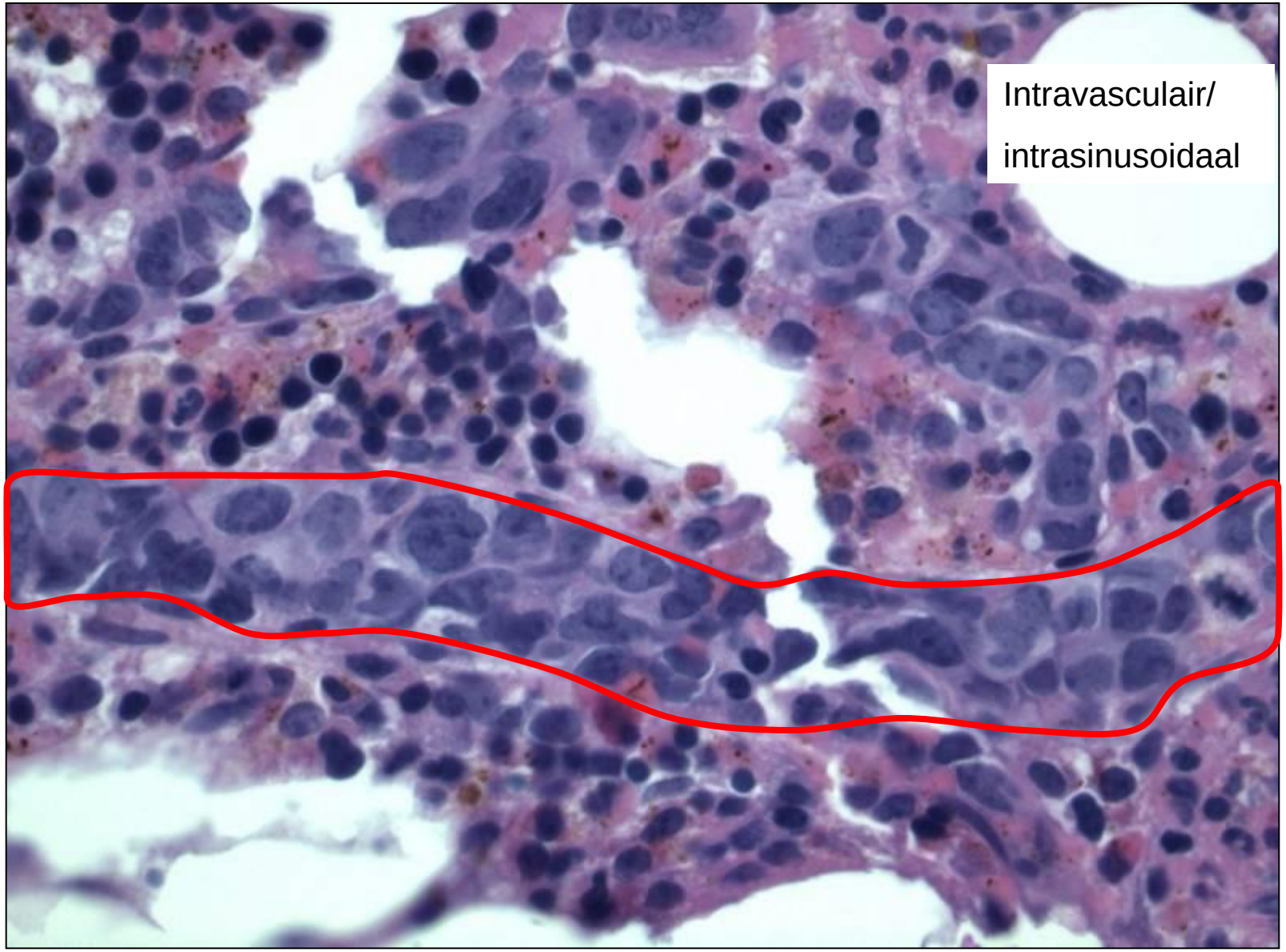
Distributie



Distributie



Distributie



Beoordeling lymfoïde infiltraten

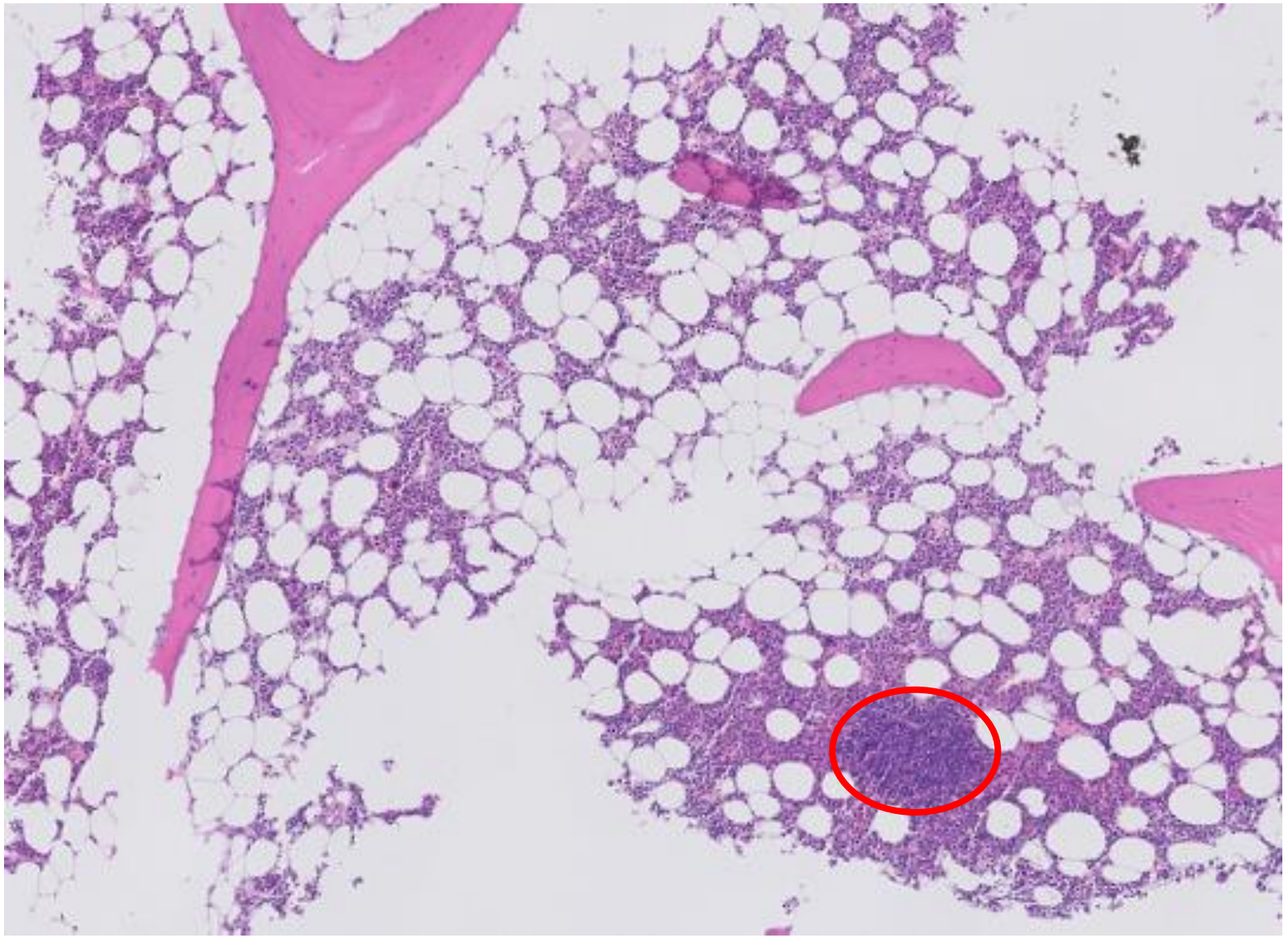
- Distributie
- Hoeveelheid
- Samenstelling (meerdere typen cellen?)
- Cellulaire morfologie (enigszins beperkt)
- Immuunhistochemie (B cellen/T cellen/specifieke markers)
- Relatie met hematopoiese, fibrose, amyloïd etc.
- Differentiaal diagnose met reactief lymfoïd infiltraat

DD reactief vs. maligne

- Reactief:
  - fysiologisch/chron.ziekte/auto-immuun/(viraal)infect
  - in context beenmergaandoening (bv. PMF, SM)

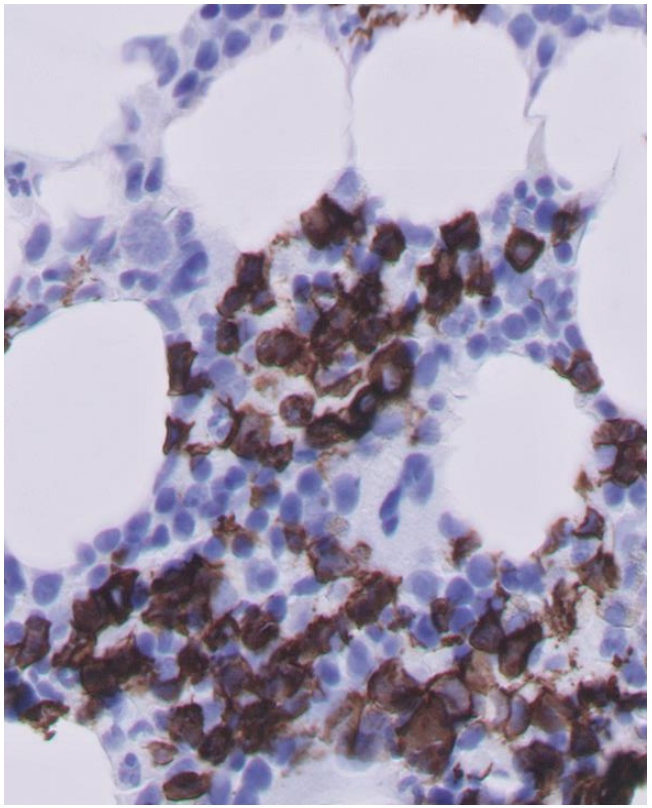
- Kenmerken reactief nodulair:
  - relatief klein en scherp begrensd
  - laag aantal nodi (neemt toe met leeftijd, v>m)
  - geassocieerd met vaatjes
  - kleine lymfocyten, T>B (T=B)
  - enkele andere cellen: plasmacel, histiocyt, mestcel, eo’s
  - soms kiemcentra

Voorbeeld reactief

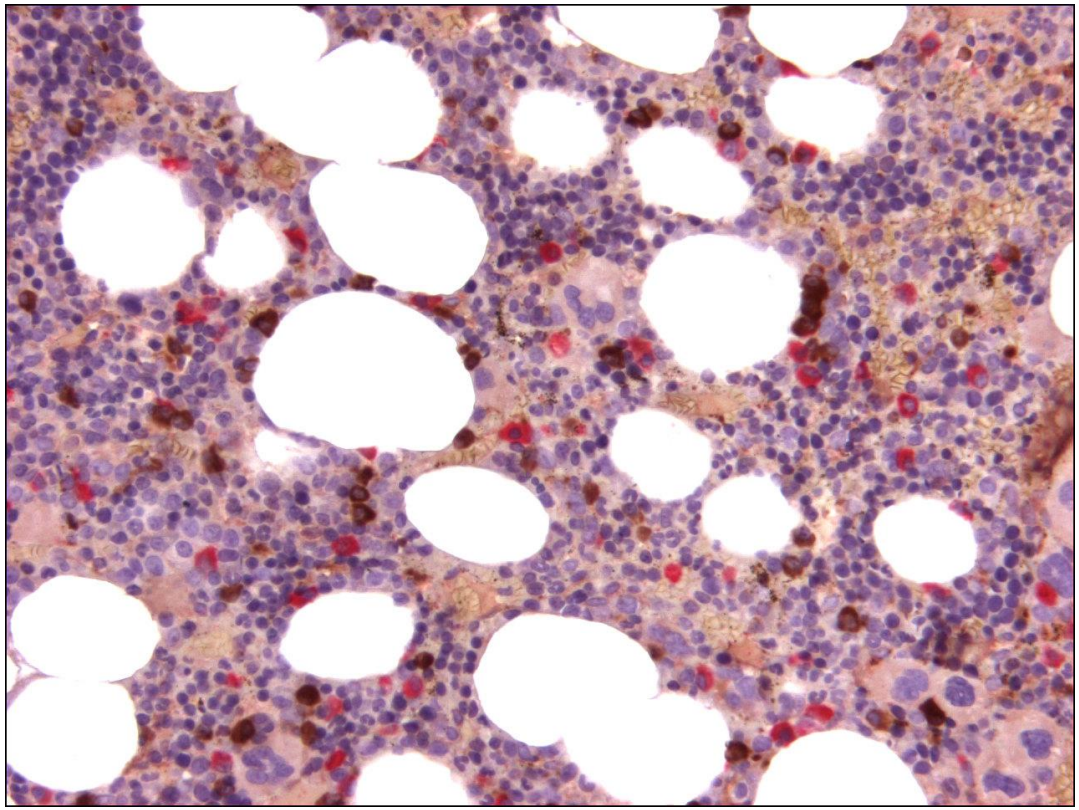


De belangrijkste immuno's voor distributie

- CD3, CD5: T-cel
- CD20, Pax-5: B-cel
- CD138: plasmacel
- kappa/lambda: clonaliteit plasmacellen

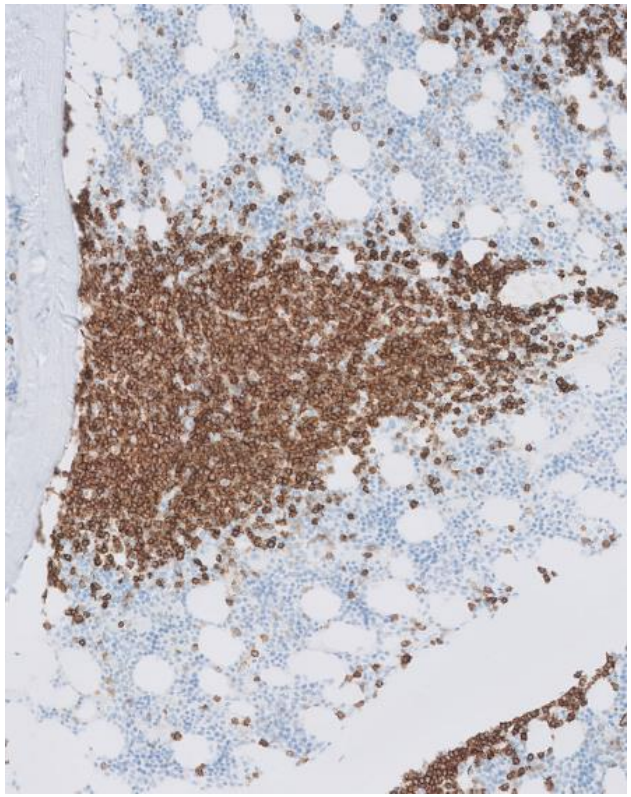


CD20

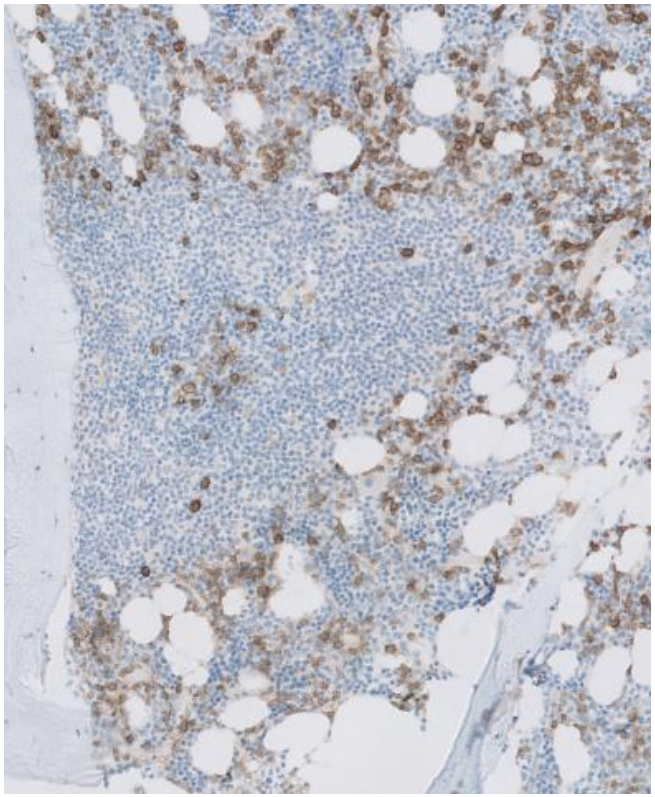


Kappa bruin / lambda rood

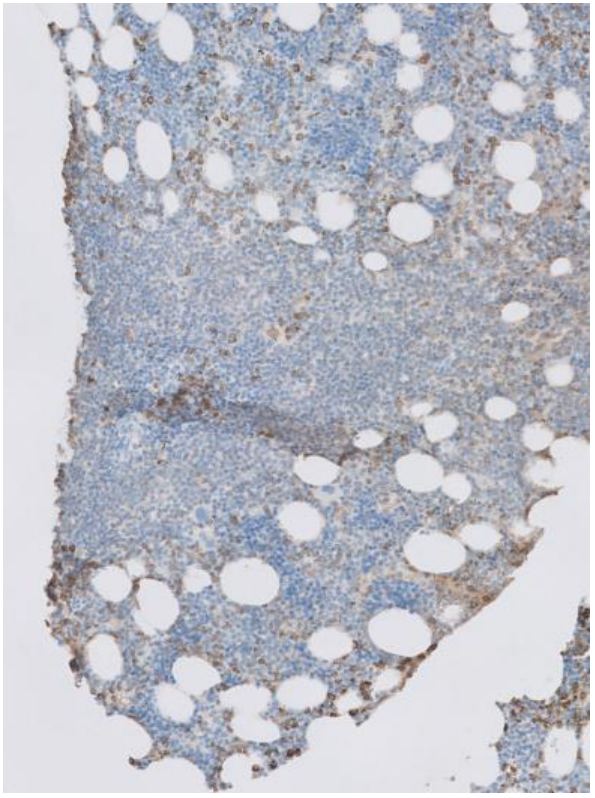
Lymfoplasmacytair lymfoom



CD20



CD138

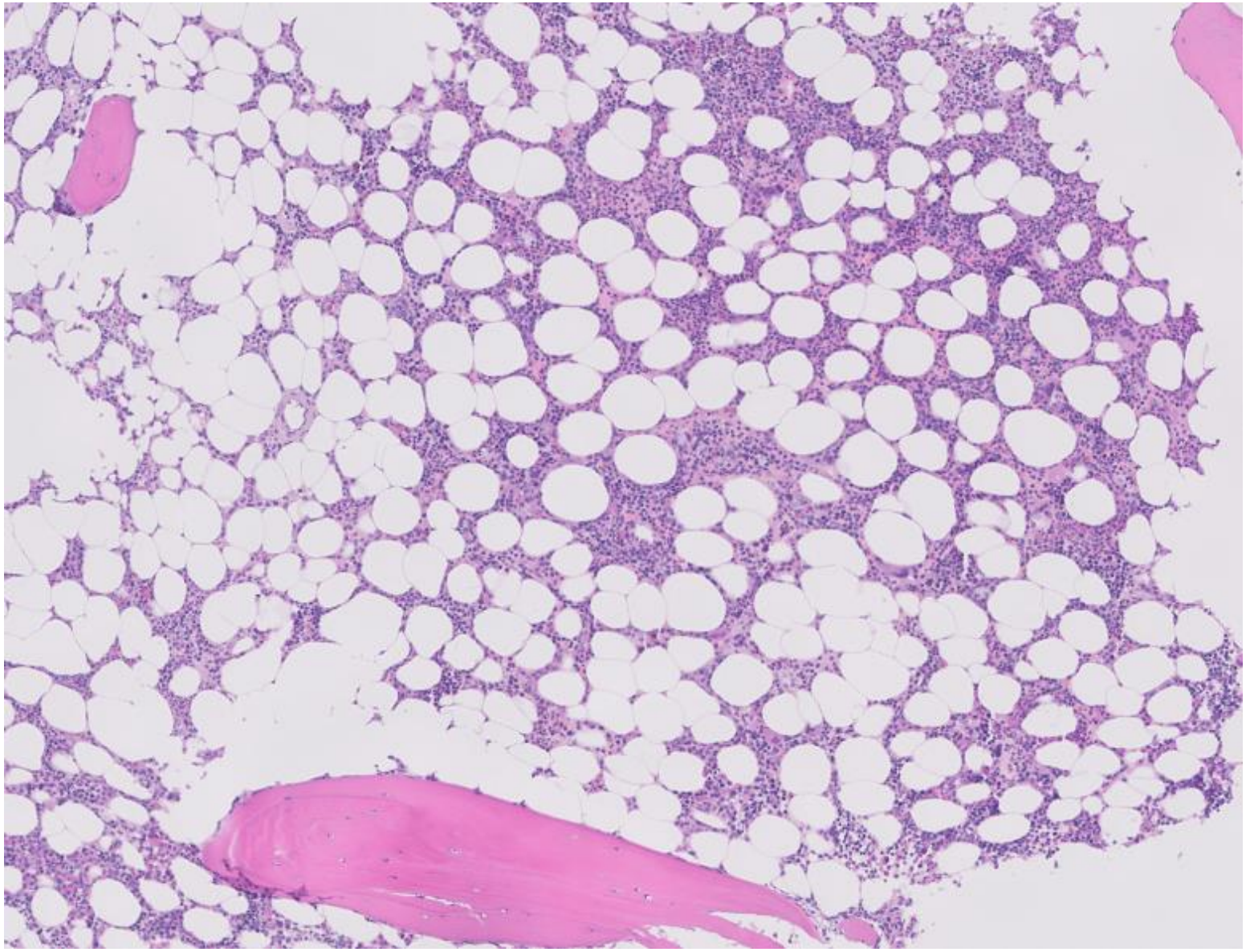


Kappa/lambda

Lymfoplasmacytair lymfoom

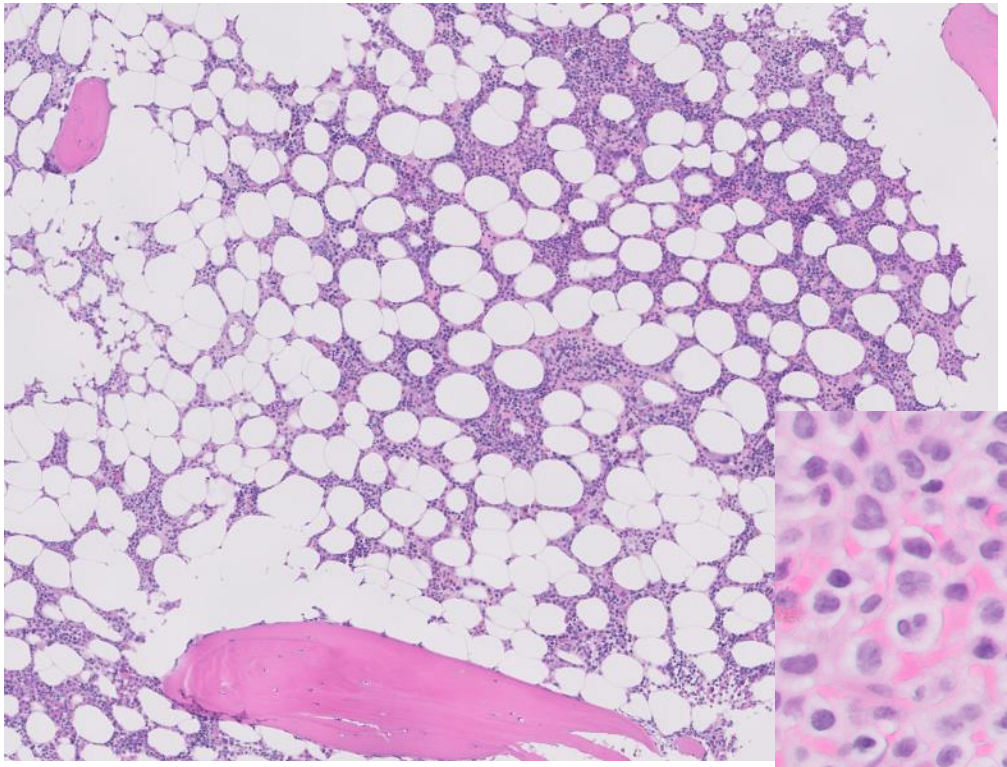
Distributie:	- nodulair, diffuus, interstitieel
Morfologie	- lymfo → plasmacytoid → plasmacel
	- veel mestcellen (Giemsa)
Immuno:	- IgM >> IgG > IgA
Genetica:	- MyD88 L265P mutatie

Lymfoom?



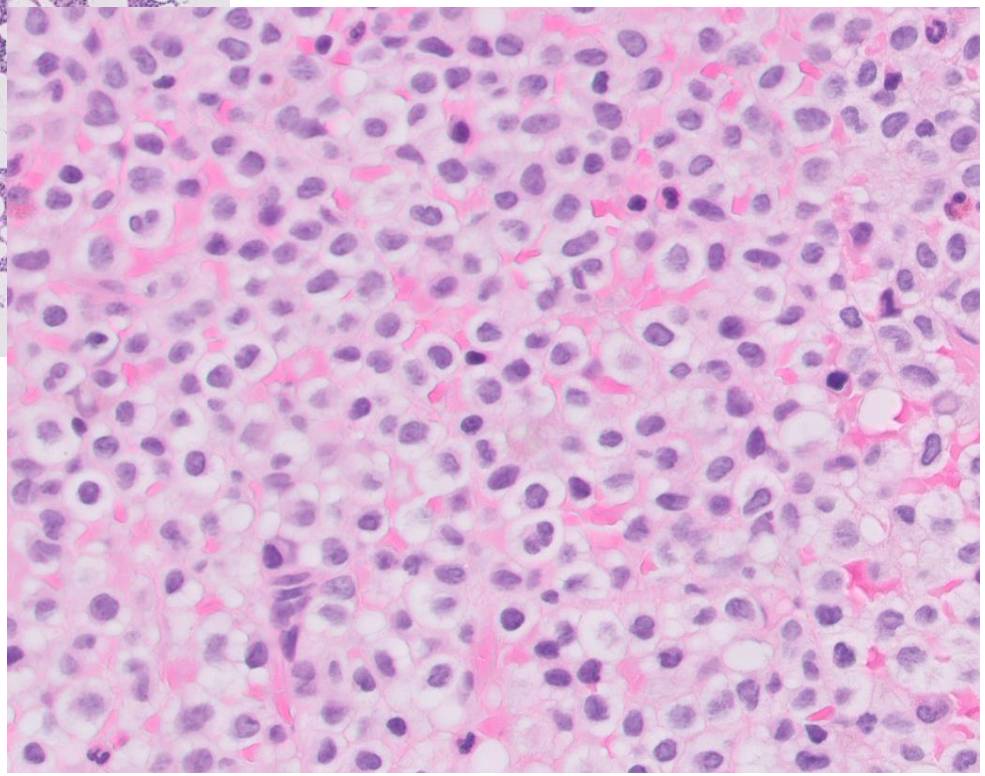
HE 5x

Hairy cell leukemie

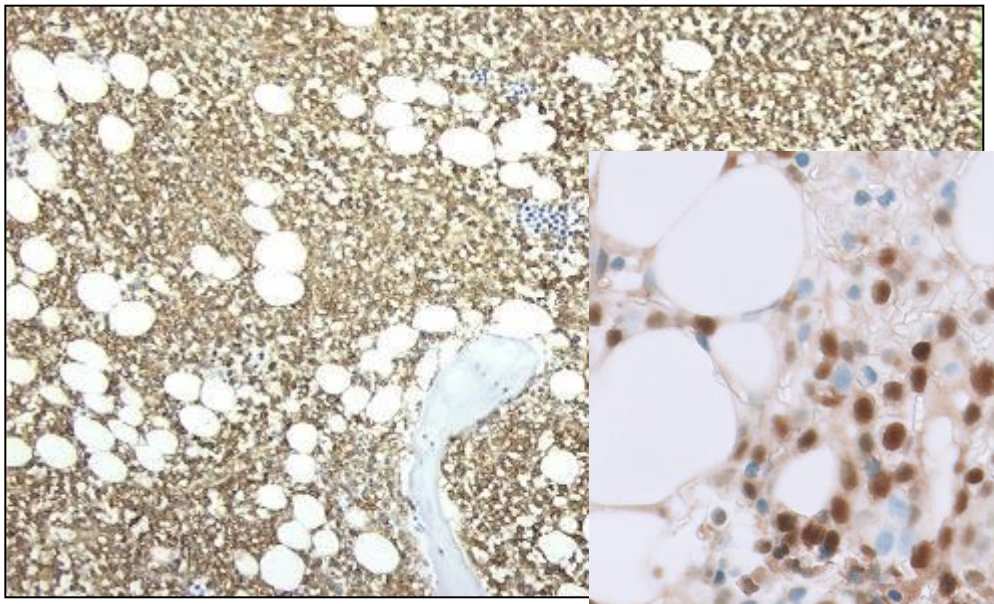


HE 5x

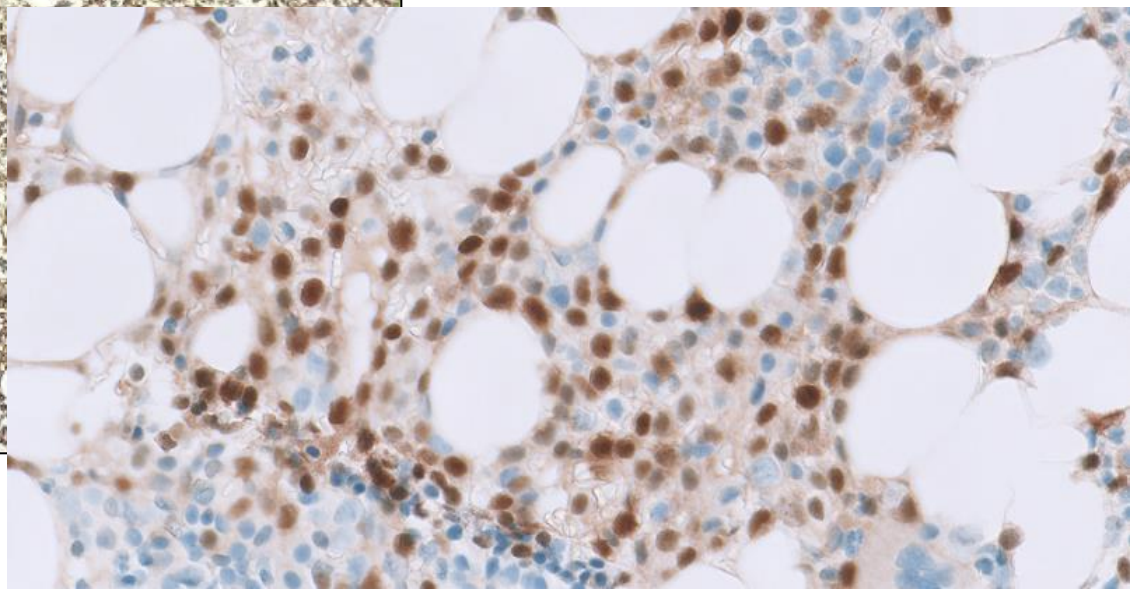
HE 40x



Hairy cell leukemie



CD20 ,5x

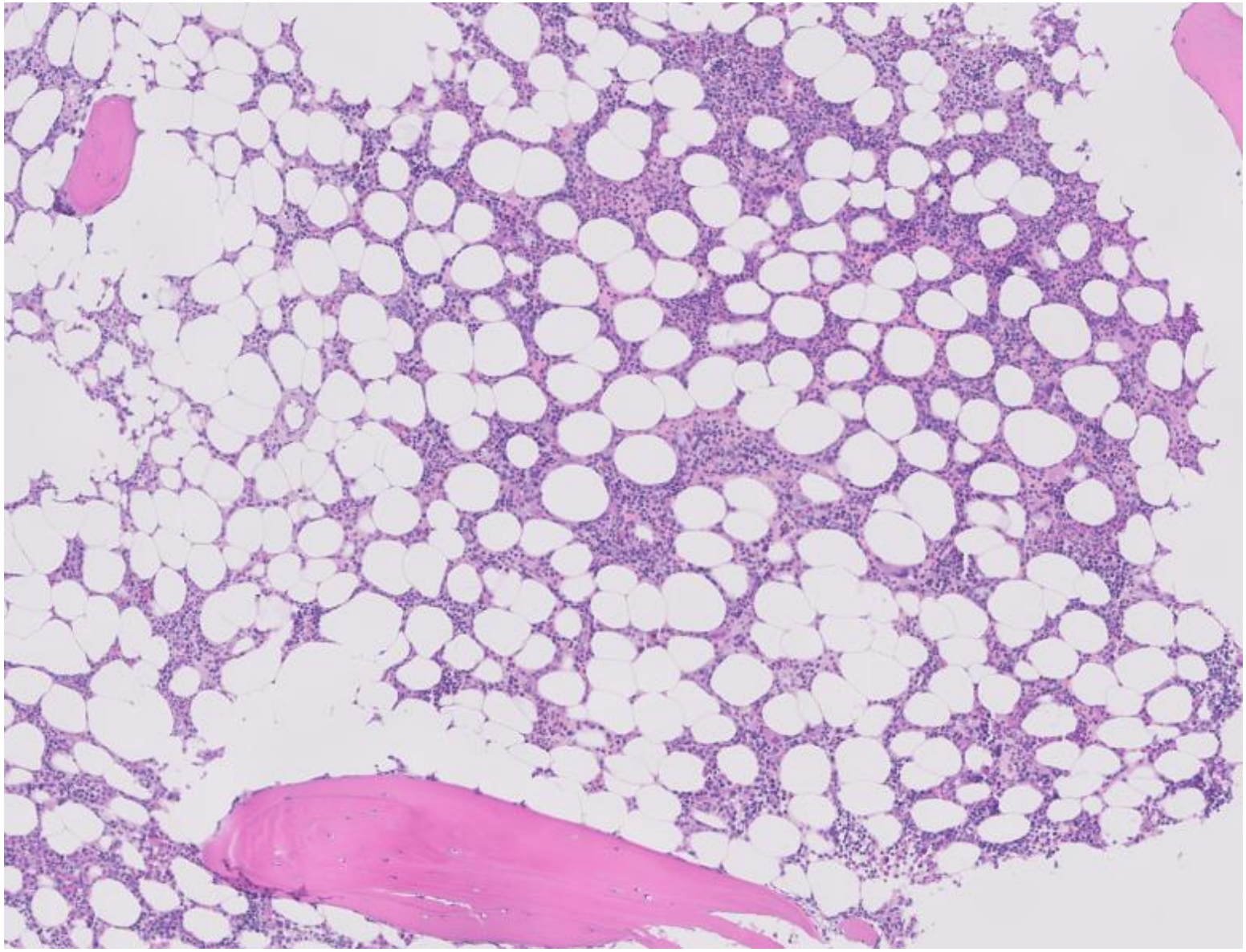


Cycline D1, 20x

Hairy cell leukemie

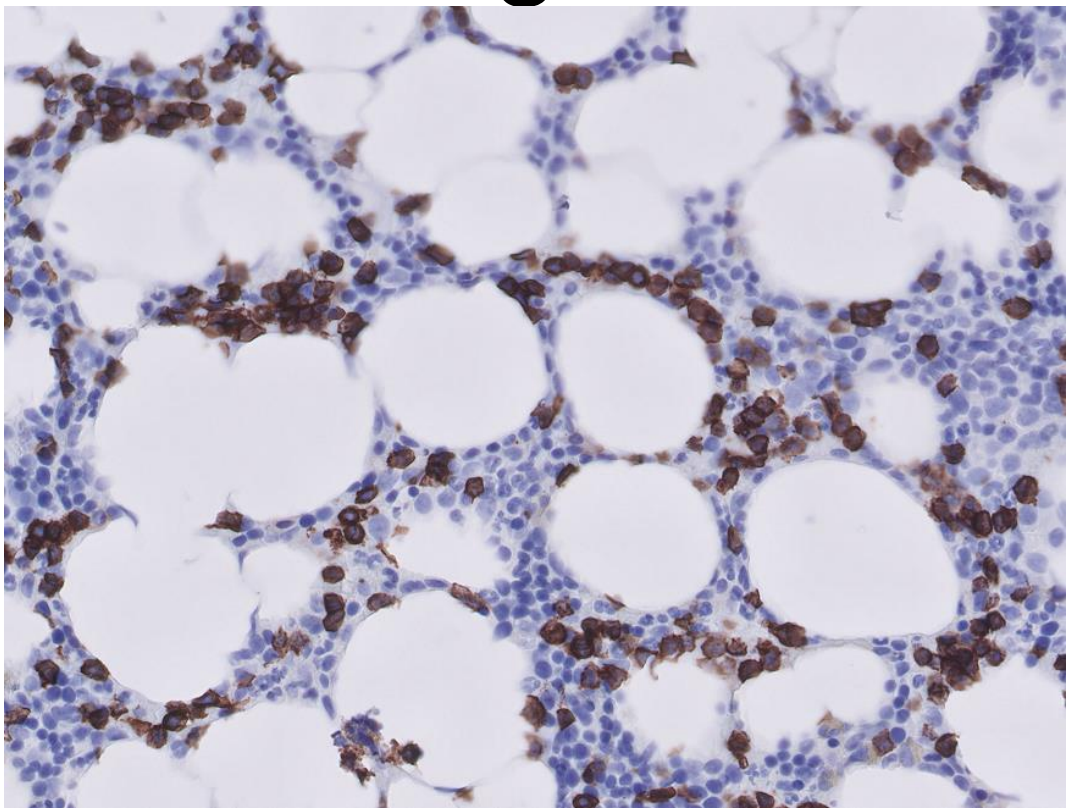
Distributie:	- interstitieel, soms richting diffuus
Morfologie	- onopvallende kleine cellen met ruim cytoplasma
	- granulopoiese afwezig, reticuline-vervezeling
	- bloedmeren
Immuno:	- CD20+
	- Cycline D1 (zwak) +
	- (Annexin A1 +)

Lymfoom?



HE 5x

Milt marginale zone lymfoom

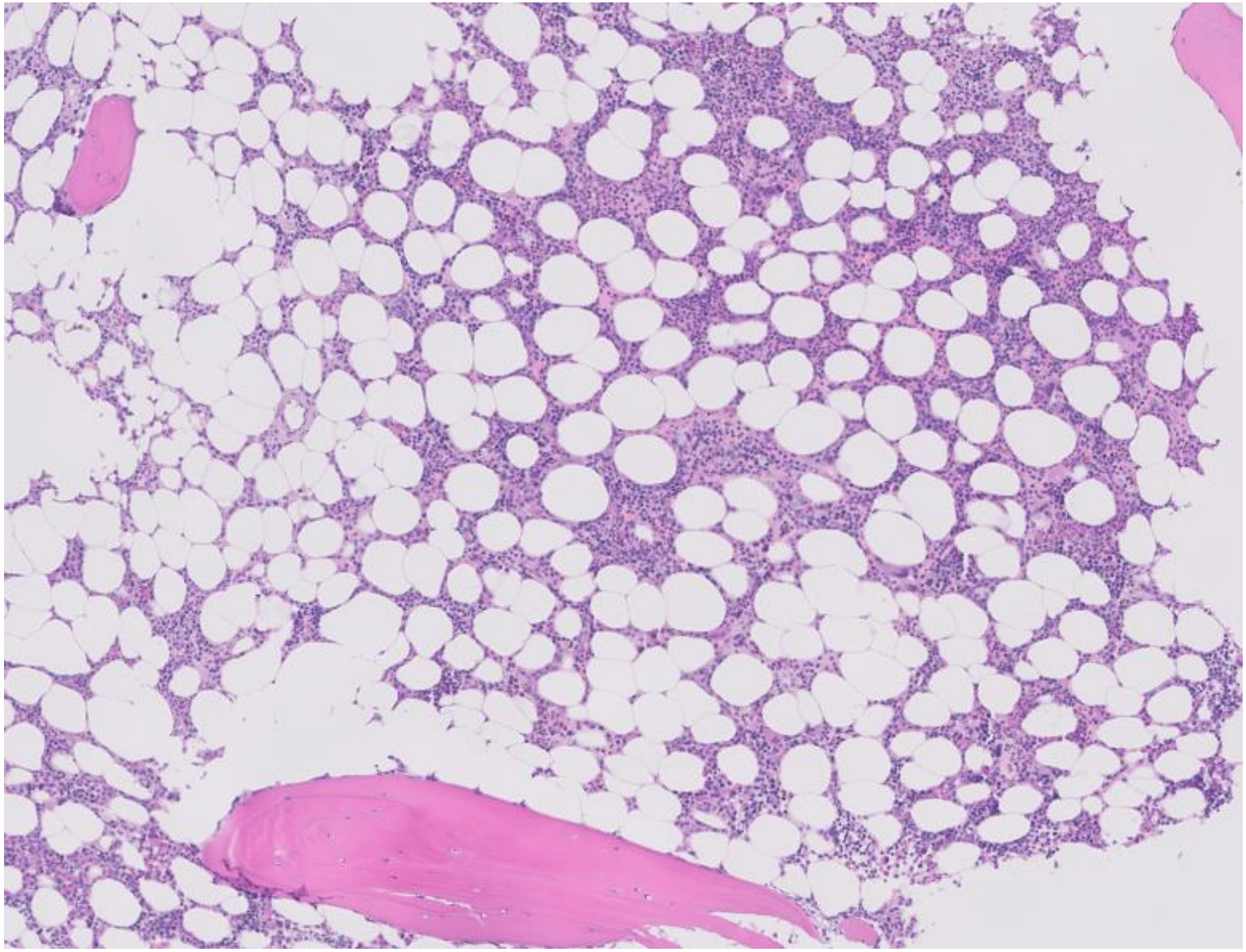


CD20 20x

Milt marginale zone lymfoom

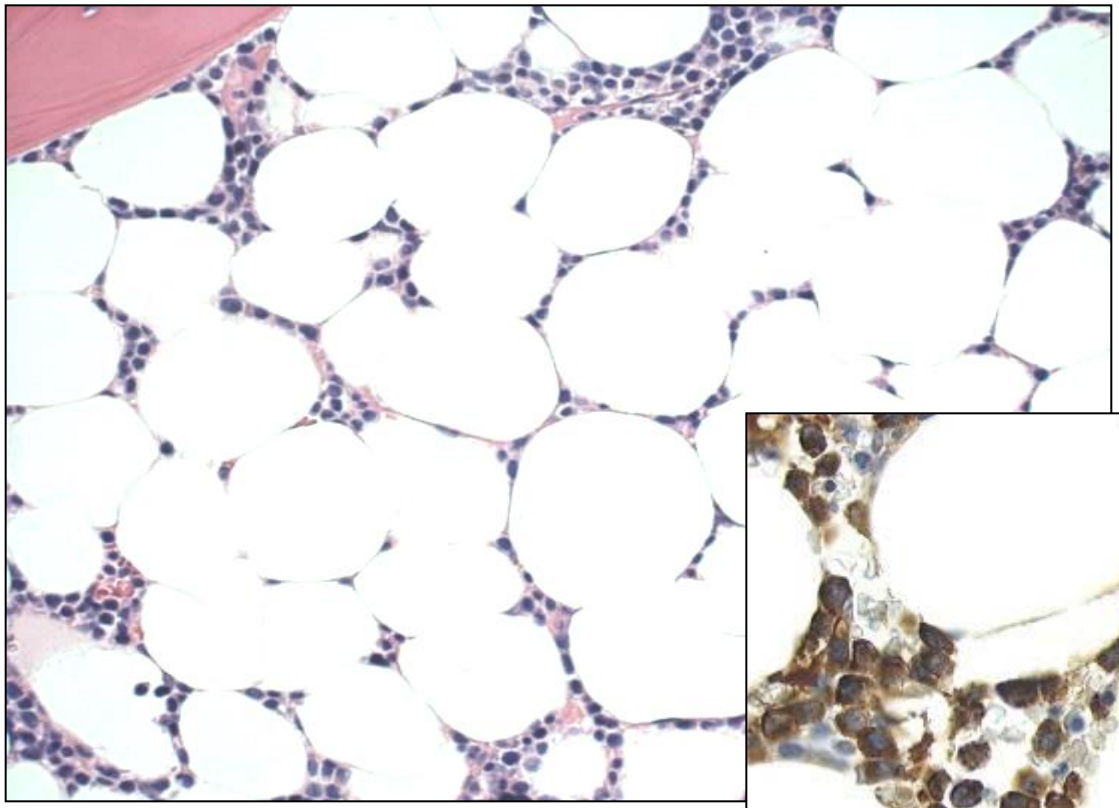
Distributie: - intravasculair en kan daarbij nodulair
Immuno: - niks specifiek

Lymfoom?

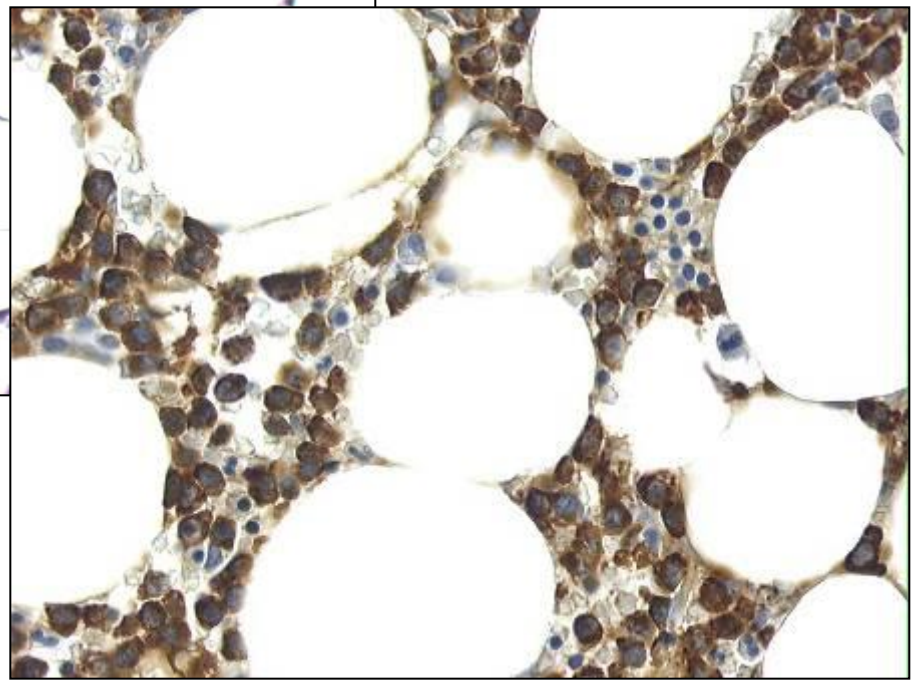


HE 5x

MGUS / multipel myeloom

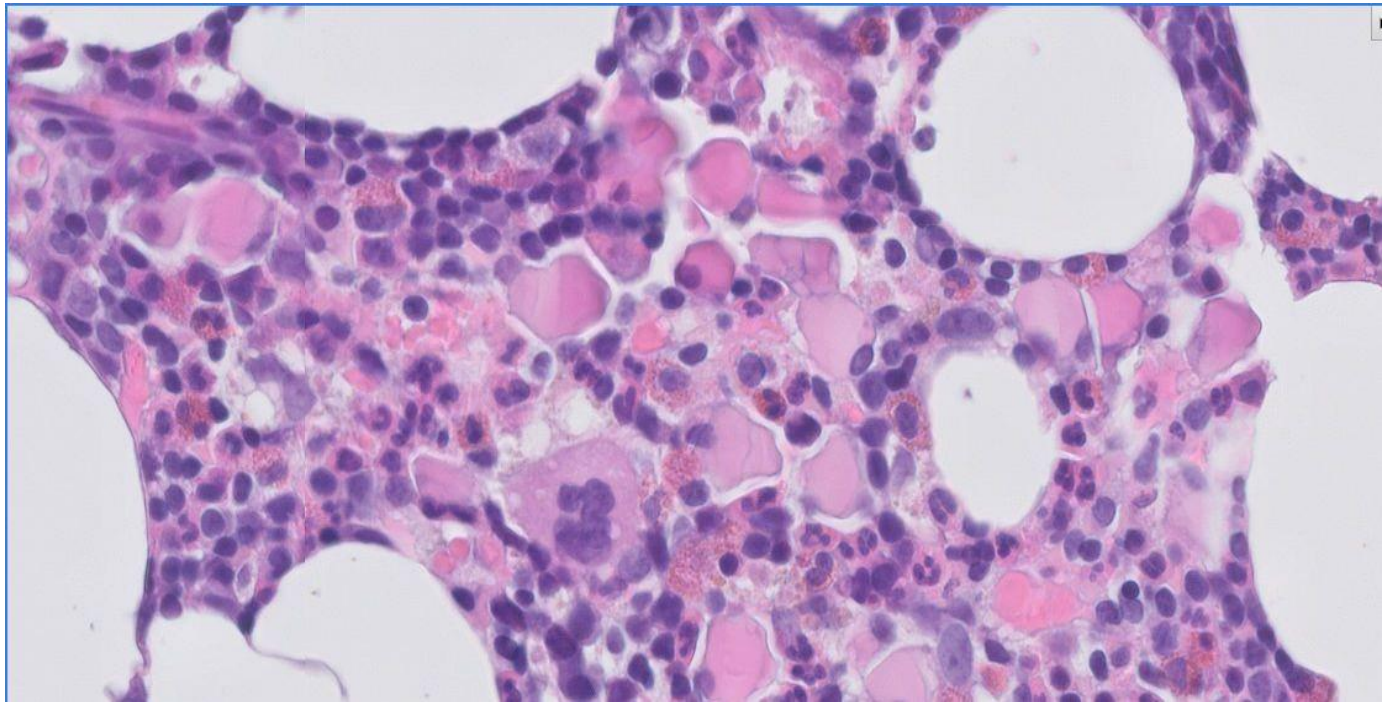


HE 10x



Kappa /lambda 40x

MGUS / multipel myeloom

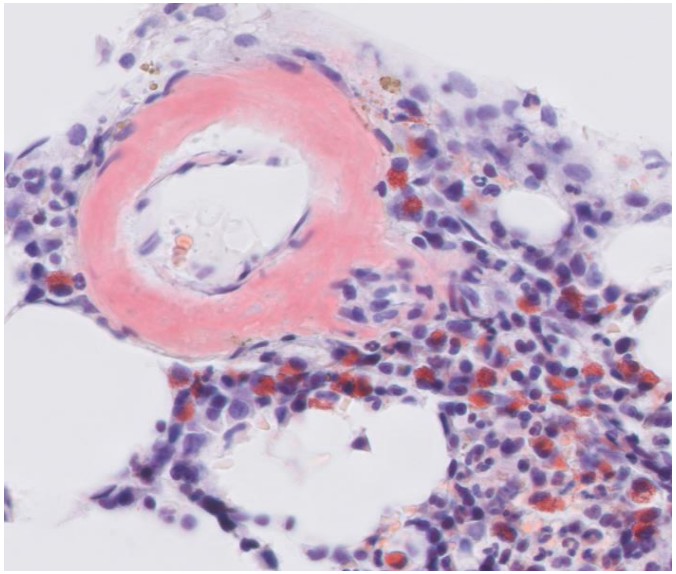


HE

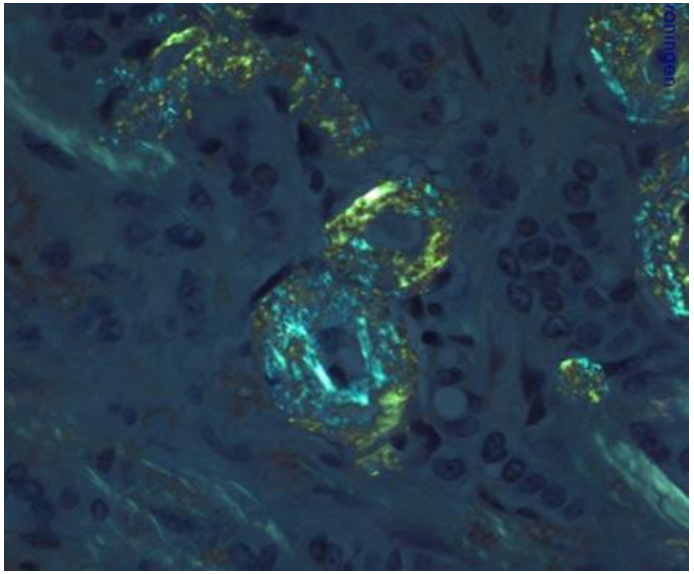
MGUS / multipel myeloom

Distributie:	- nodulair, interstitieel, diffuus
Morfologie	- (atypische) plasmacel, Dutcher, Russell
Immuno:	- CD138, CD79a
	- kappa/lambda, IgG en IgA en xIg >> IgD, IgE, IgM
	- soms: CD20+, Cycline D1+, CD56+, CD117+, CD10+

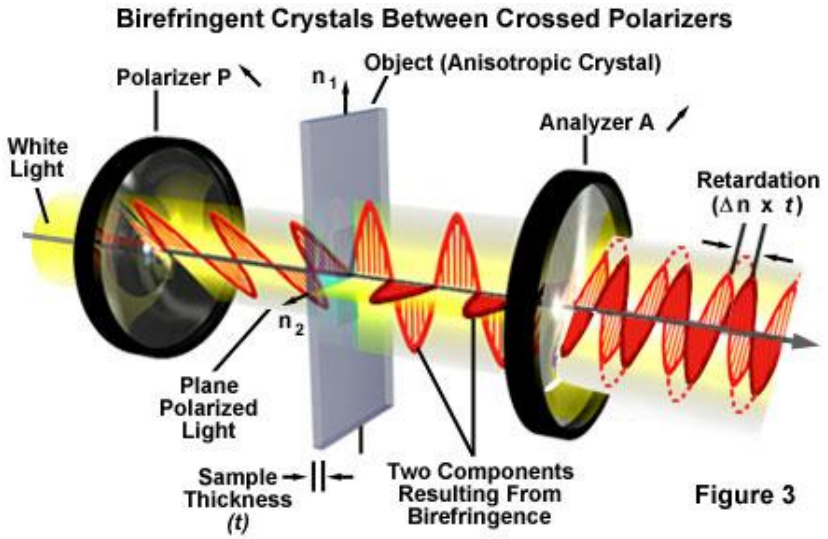
MGUS / multipel myeloom



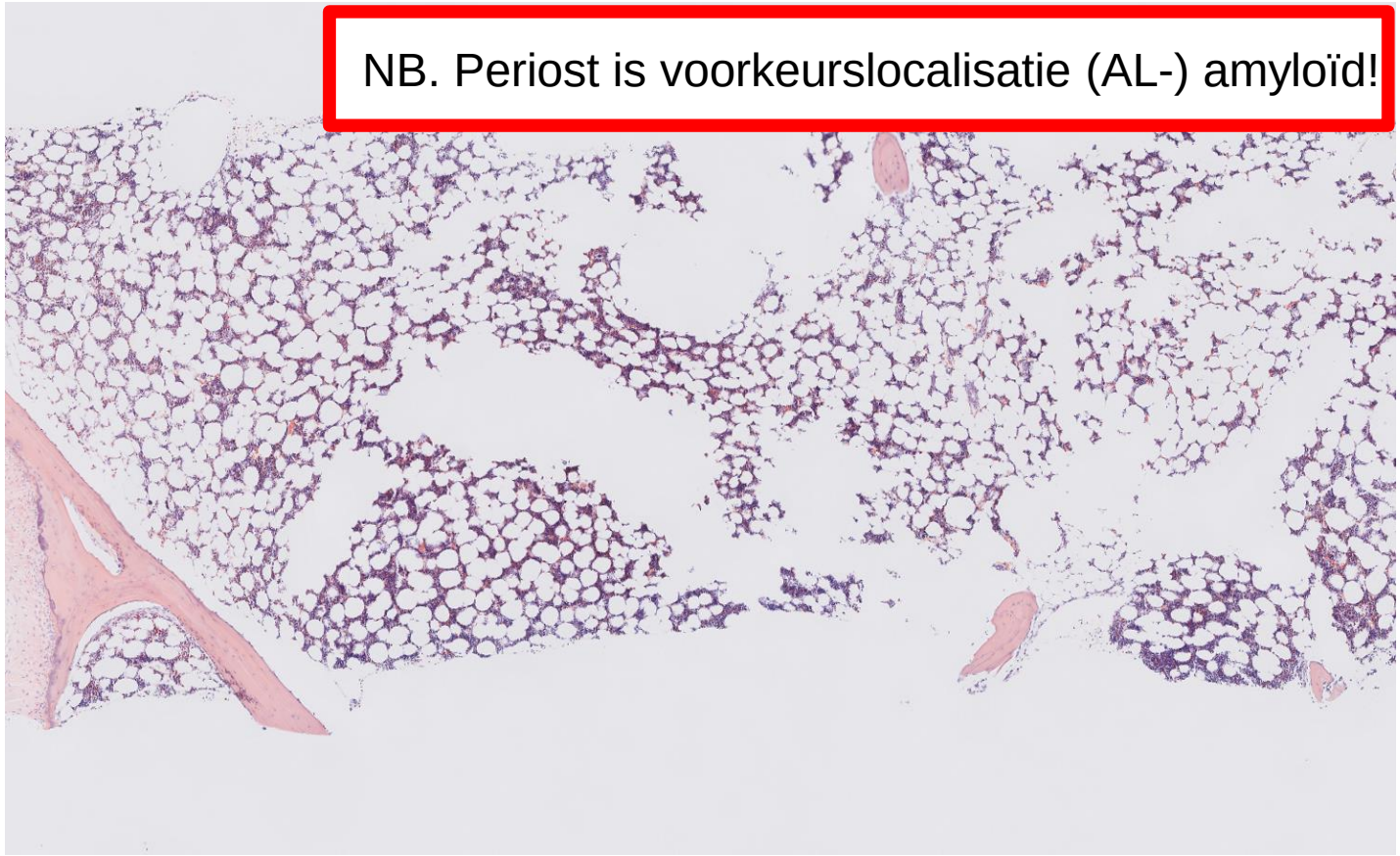
Amyloid, Congorood



Amyloid, Congorood, dubbelbreking

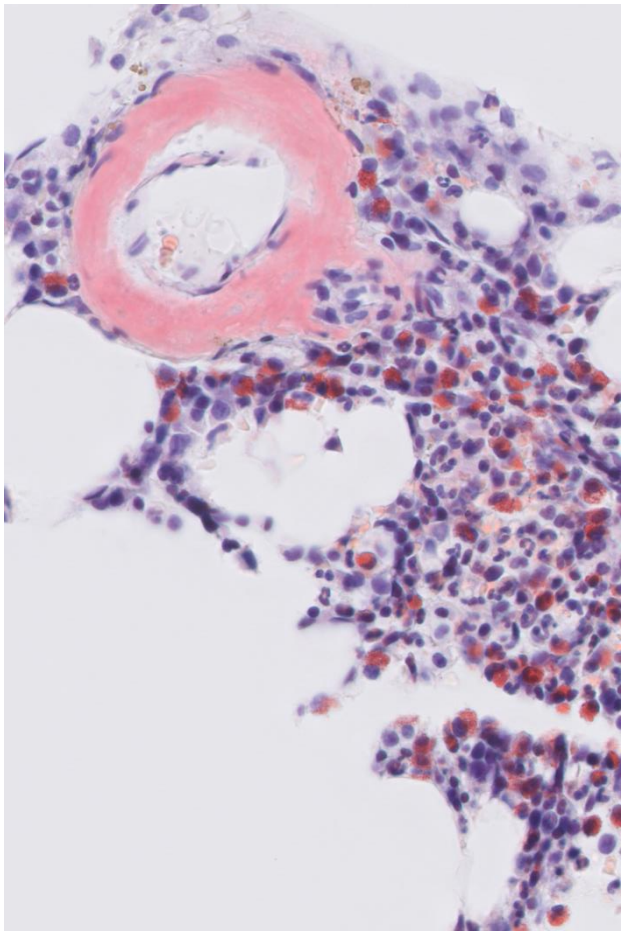


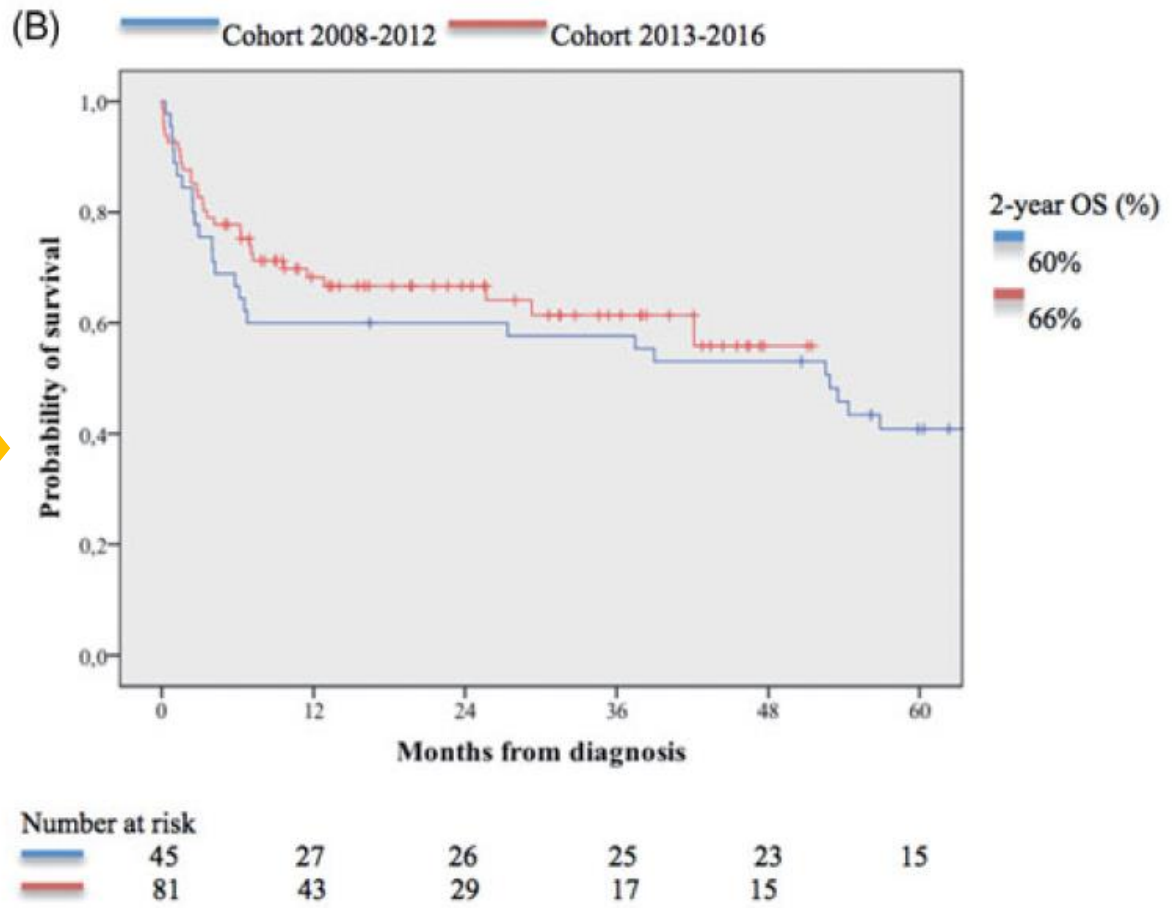
MGUS / Multipel myeloom



Lichte keten (AL) amyloidose

80% MGUS, 15% Multipel myeloom, 5% LPL

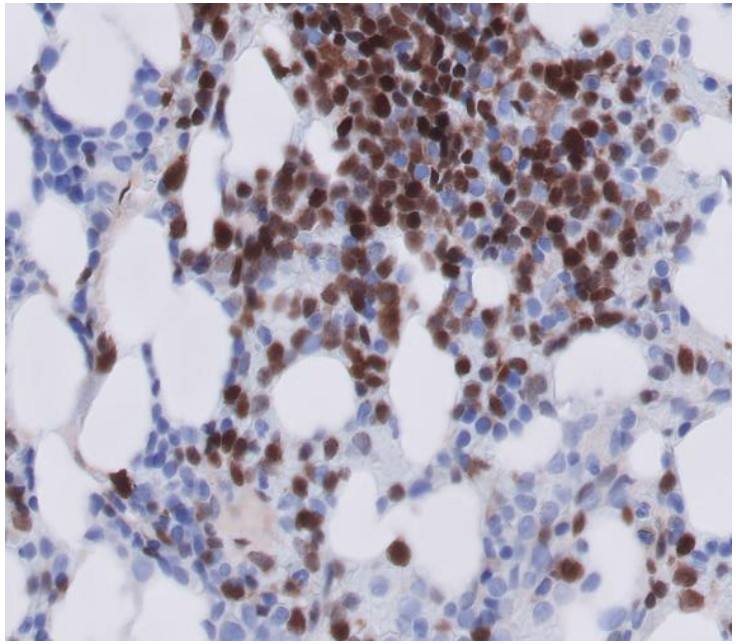




Rutten et al. Amyloid 2018

Overige belangrijke immuno’s in BM

- CLL/SLL: CD5+(zwak), CD23+/-, Cycline D1-
- Mantelcel: CD5+, CD23-, Cycline D1+, SOX-11+
- DLBCL: CD20+, Pax-5+, TdT-
- Lymfoblastair: B/T+, TdT+



Cycline D1

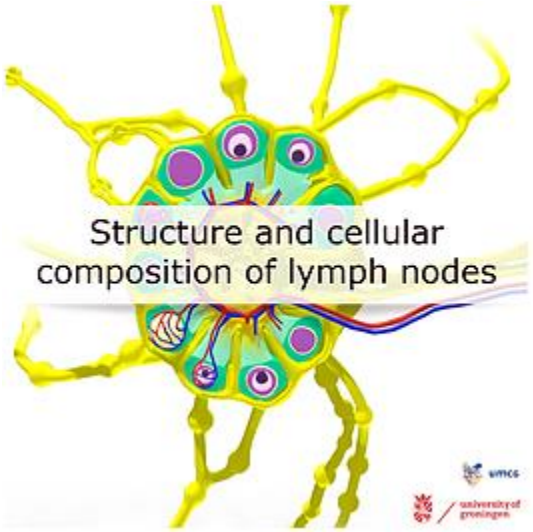
Grootcellige lymfomen in BM?

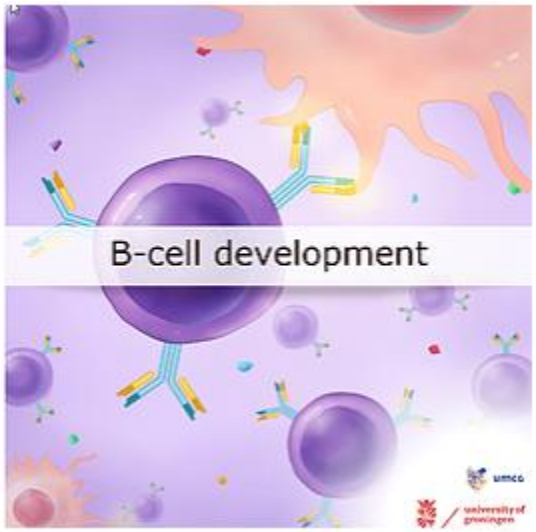
- Tumorcellen tenminste 2x zo groot als normale lymfocyt
- Diffuus grootcellig B cel lymfoom (nodulair, diffuus)
- Burkitt lymfoom / lymfoblastair lymfoom (diffuus)
- Hodgkin lymfoom (grote haarden)
- Anaplastisch grootcellig T-cel lymfoom (nod.,int.,diffuus)
- NB1. Soms ook enkele grote cellen bij kleincellig
- NB2. Grote cellen zijn niet altijd lymfoom

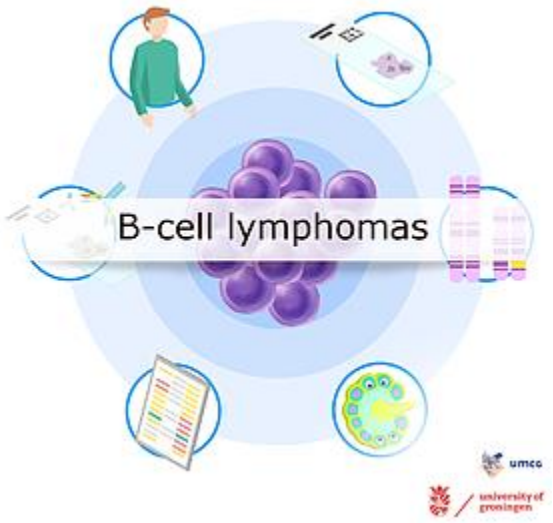
Conclusie / opmerkingen

- Goede biopten belangrijk, stagering 2 cm!
- Respons op behandeling? → vergelijk
- Patroonherkenning
- Volledige beenmergbeoordeling
- Immunohistochemie pitfalls
- Classificatie in principe beste op lymfklier
- Discordantie mogelijk

Achtergrond B-cel lymfomen







www.lymphomaresearchgroningen.nl

tabblad “Media” -> “E-learning”


TIME FOR QUESTIONS