

# Hersentumoren bij kinderen

Betere behandeling door innovatie in research en zorg



prinses  
**MÁXIMA**  
centrum voor kinderoncologie

Presentatie  
VOKK

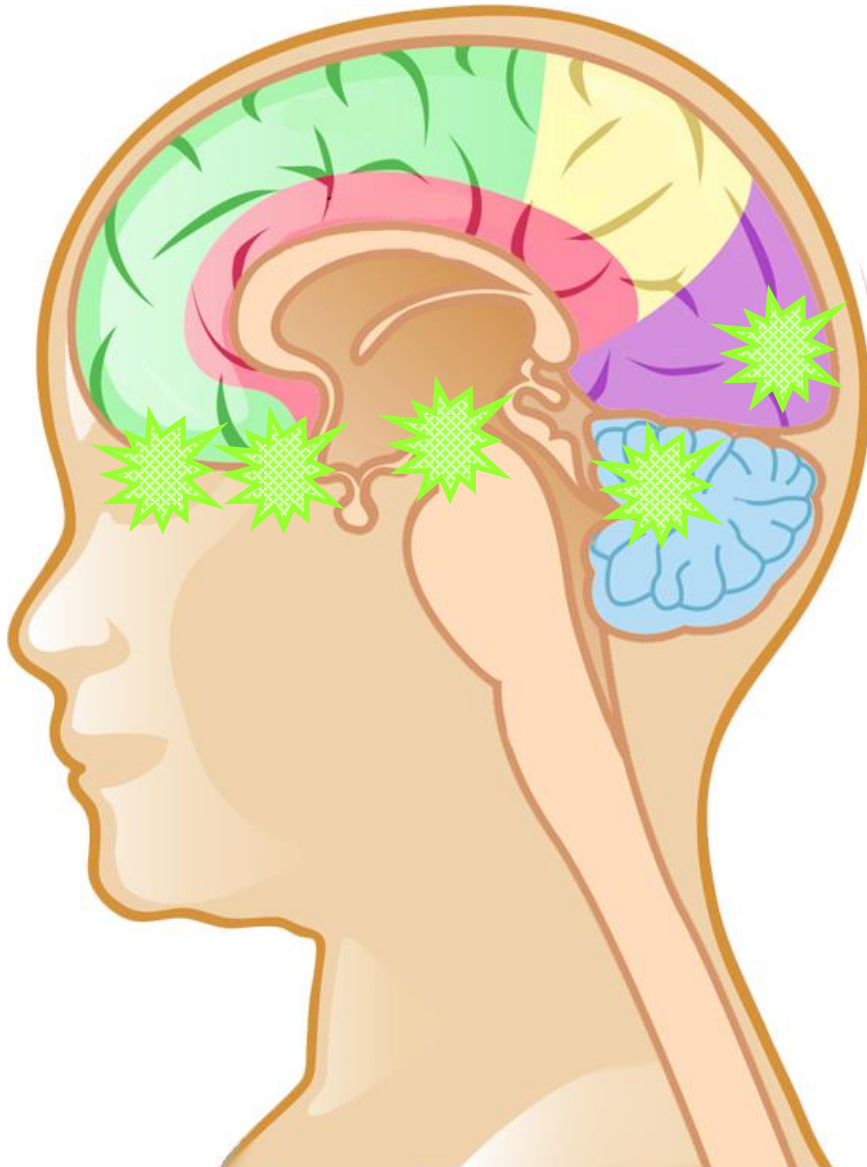
Dr. Dannis van Vuurden

# Hersentumoren op kinderleeftijd

- 120 kinderen per jaar in Nederland
- Na leukemie meest voorkomende vorm van kinderkanker
- Veel verschillende soorten
- Zeldzame ziektebeelden
- Relatief hoge sterfte
- Veel late effecten, matige kwaliteit van leven



# Laaggradig glioom (LGG)



24-36 kinderen per jaar in NL

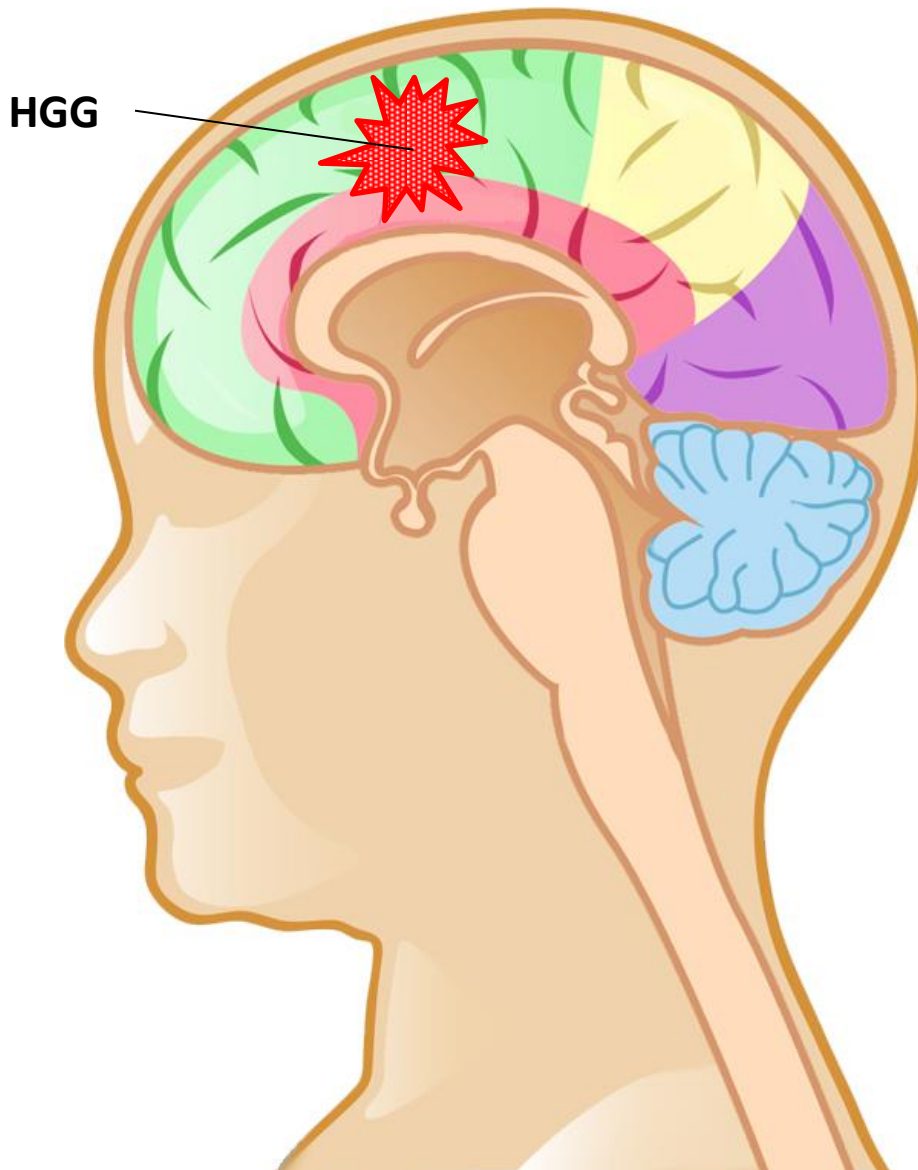
Behandeling:

- Operatie
- Chemotherapie
- Radiotherapie
- Wait and see

5-jaars overleving 90-95%



# Hooggradig glioom (LGG)



8 kinderen per jaar in NL

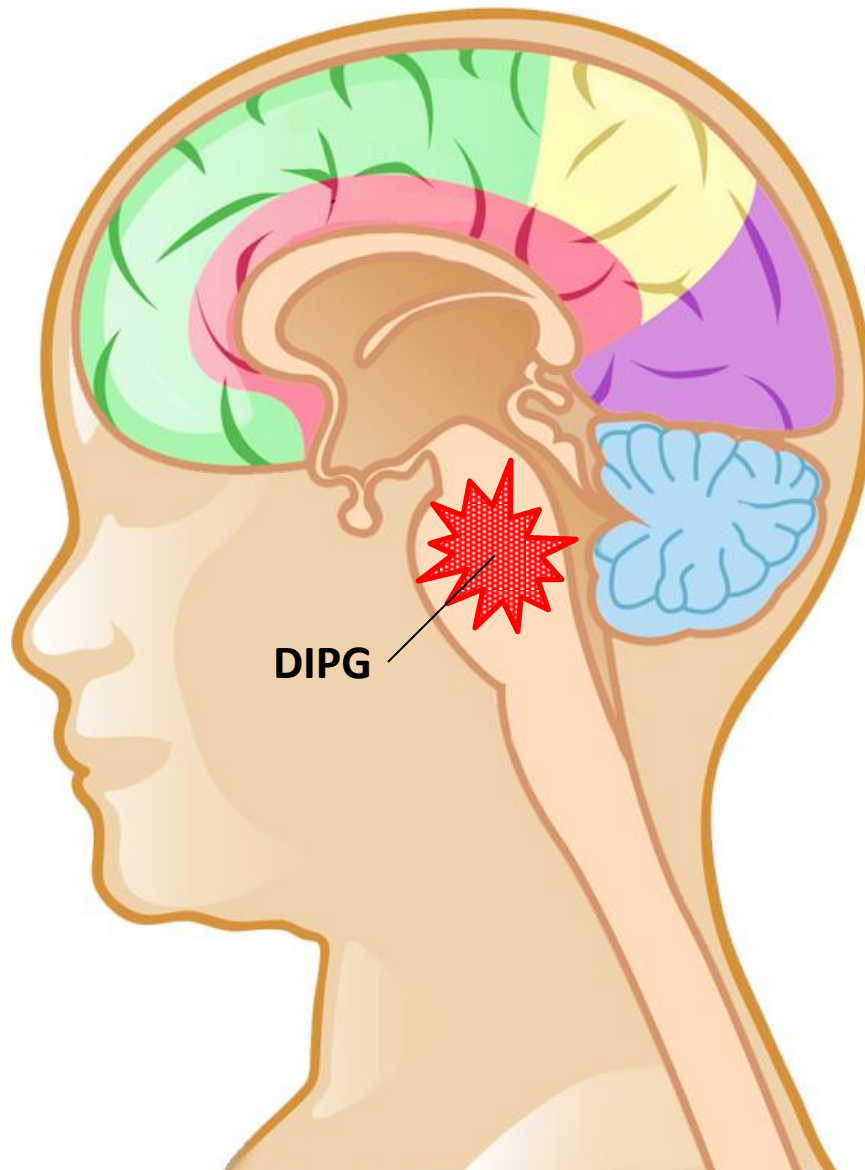
Behandeling:

- Operatie
- Radio/chemotherapie
- Chemotherapie

5-jaars overleving 25%



# Diffuus intrinsiek ponsglioom (DIPG)



5 - 8 kinderen per jaar in NL

Ook wel: *diffuus midlijn glioom met histon mutatie*

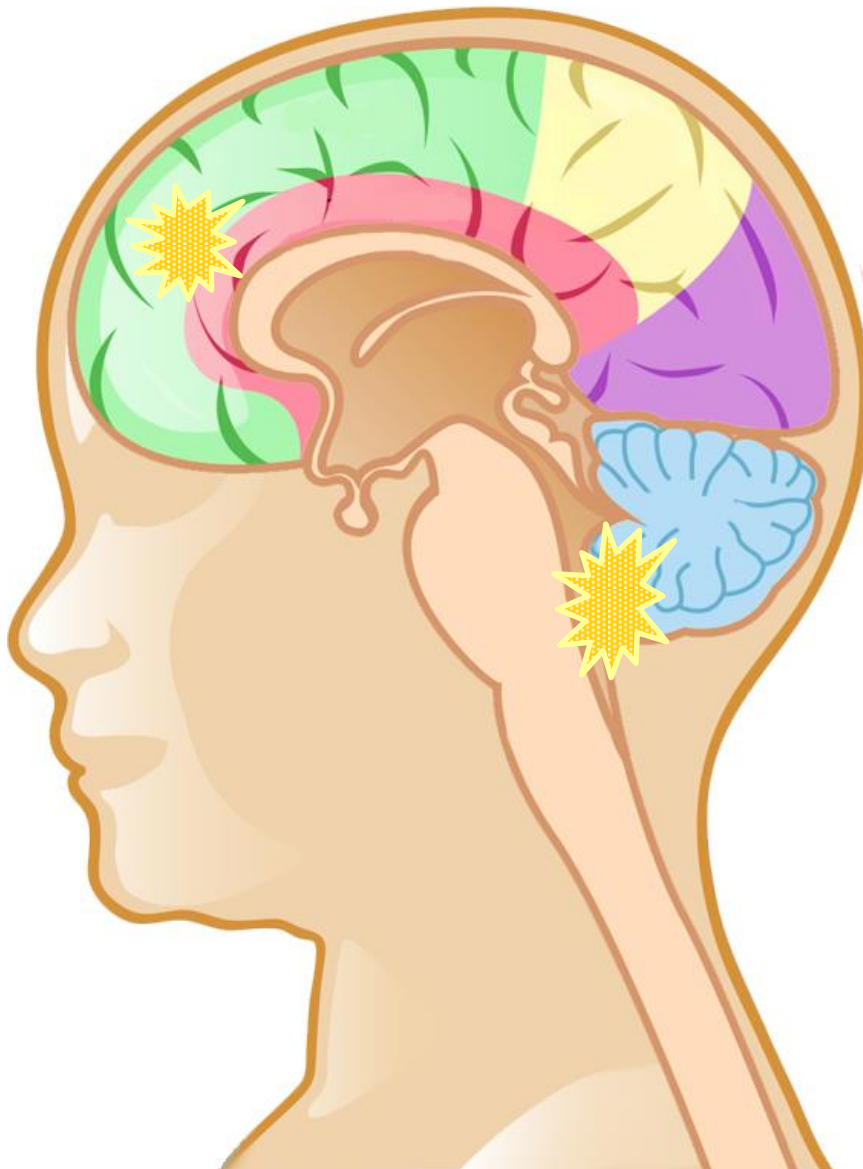
Behandeling:

- Operatie
- Radio/chemotherapie
- Chemotherapie

5-jaars overleving 2%



# Ependymoom



10 – 12 kinderen per jaar in NL

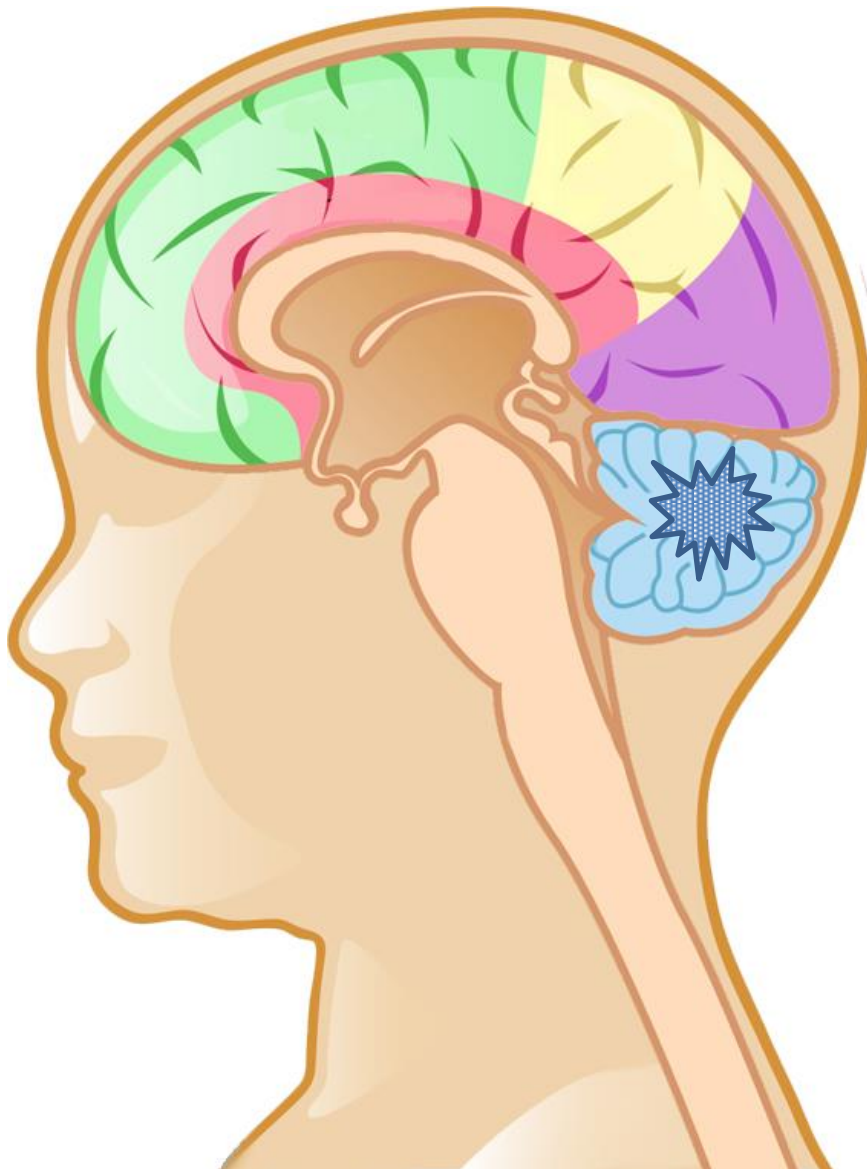
Behandeling:

- Operatie
- Radiotherapie
- (Chemotherapie)

5-jaars overleving 50-60%



# Medulloblastoom



18 – 24 kinderen per jaar in NL

Behandeling:

- Operatie
- Radio/chemotherapie
- Chemotherapie

5-jaars overleving

70-80%



# Geïntegreerde multidisciplinaire zorg

Neurochirurgie  
Kinderoncologie  
Kinderneurologie

Pathologie

Radiotherapie

Endocrinologie

Oogheelkunde

Revalidatie, fysiotherapie

Radiologie

Audiologie

(Neuro)psychologie

Neuropsychologie

Verpleegkundigen

Psychosociaal team

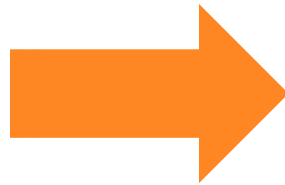




# Innovatieve research – bench to bedside

Relatief hoge sterfte

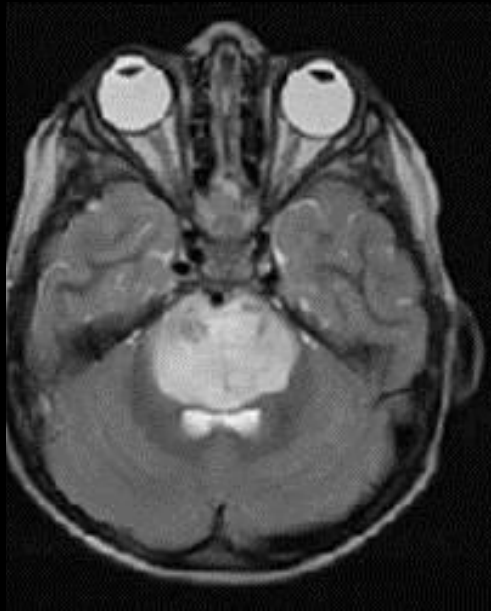
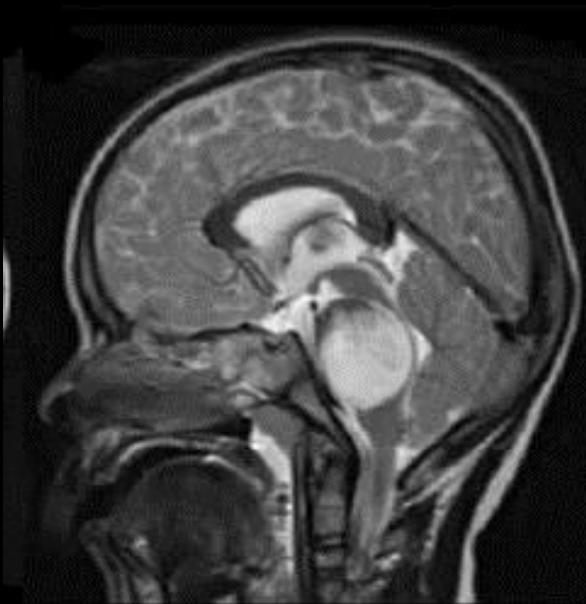
Veel late effecten, matige kwaliteit van leven

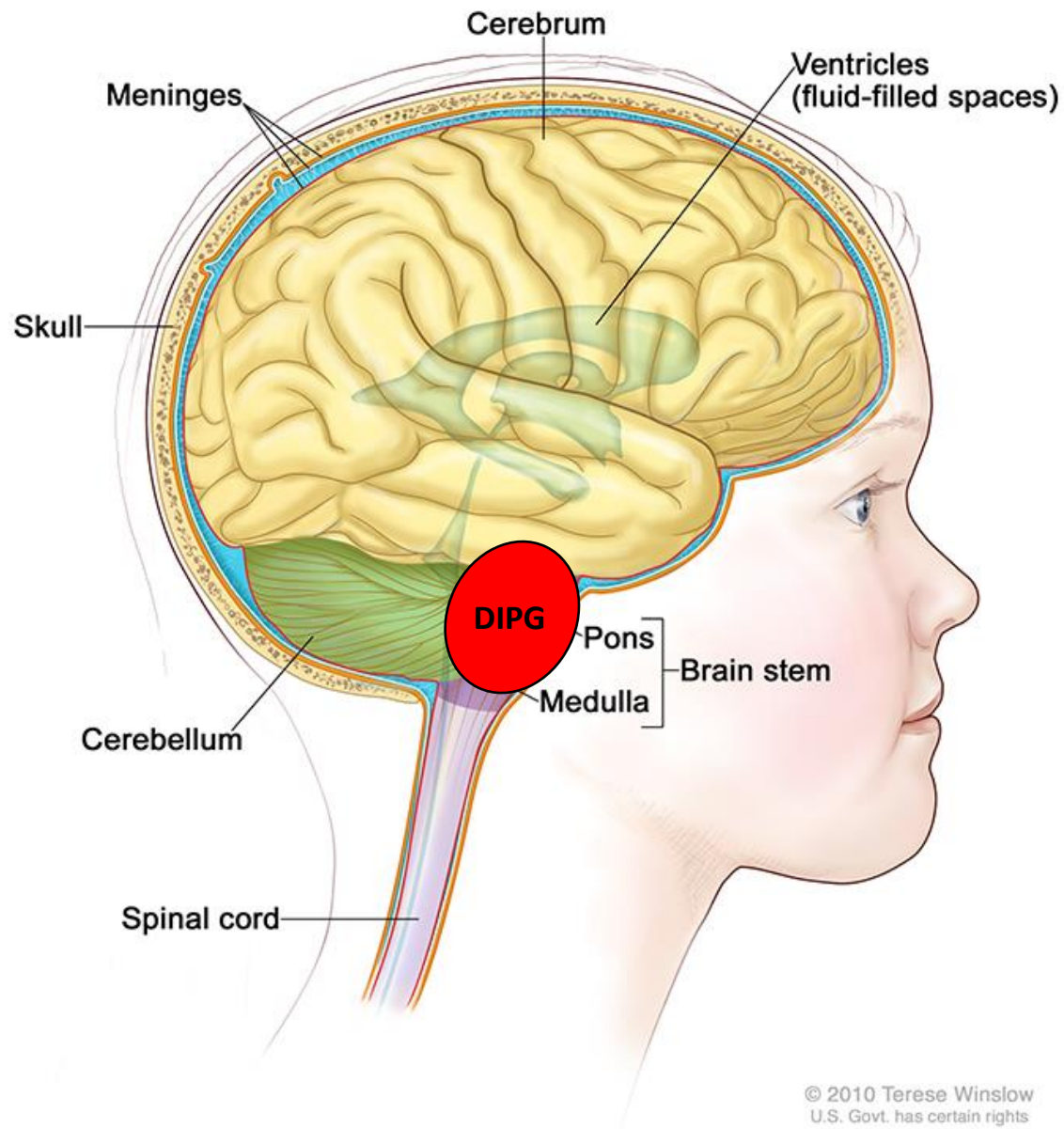


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# Diffuus Intrinsiek Pongsglioom (DIPG)

- Per jaar 10 kinderen in NL, 400 kinderen in Europa
- Geen genezing
- Snelle neurologische achteruitgang

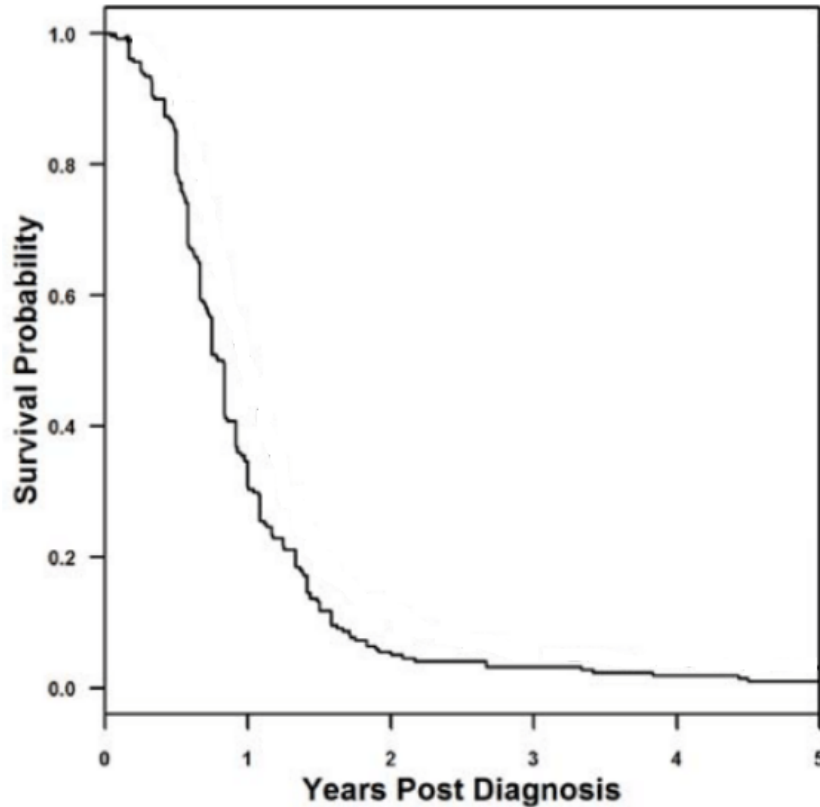




# DIPG – Operatie onmogelijk



# DIPG – geen kans op genezing



Sophie E.M. Veldhuijzen van Zanten et al. JCO 2018

# DIPG in het laboratorium 'goed' te behandelen

OPEN ACCESS Freely available online

PLOS ONE

## *In Vitro* Drug Response and Efflux Transporters Associated with Drug Resistance in Pediatric High Grade Glioma and Diffuse Intrinsic Pontine Glioma

Susanna J. E. Veringa<sup>1,2</sup>, Dennis Biesmans<sup>1,2</sup>, Dannis G. van Vuurden<sup>1,2</sup>, Marc H. A. Jansen<sup>1</sup>, Laurine E. Wedekind<sup>2,5</sup>, Ilona Horsman<sup>3</sup>, Pieter Wesseling<sup>4,6</sup>, William Peter Vandertop<sup>5</sup>, David P. Noske<sup>2,5</sup>, GertJan J. L. Kaspers<sup>1</sup>, Esther Hulleman<sup>1,2\*</sup>



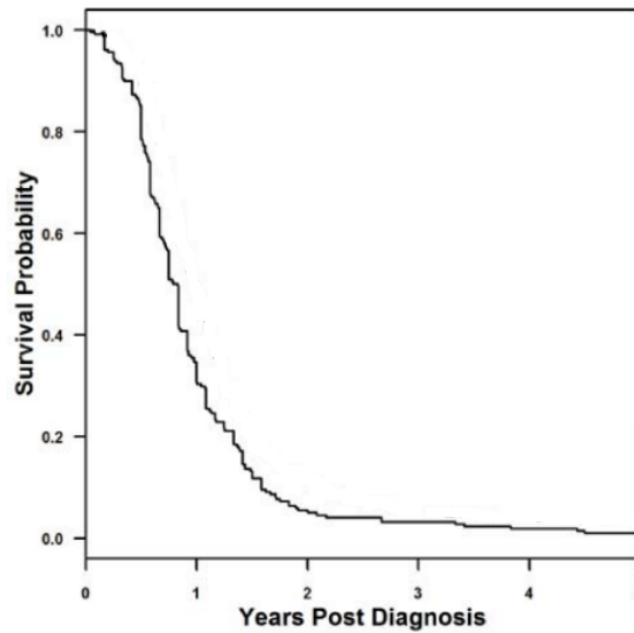
nature  
medicine

## Functionally defined therapeutic targets in diffuse intrinsic pontine glioma

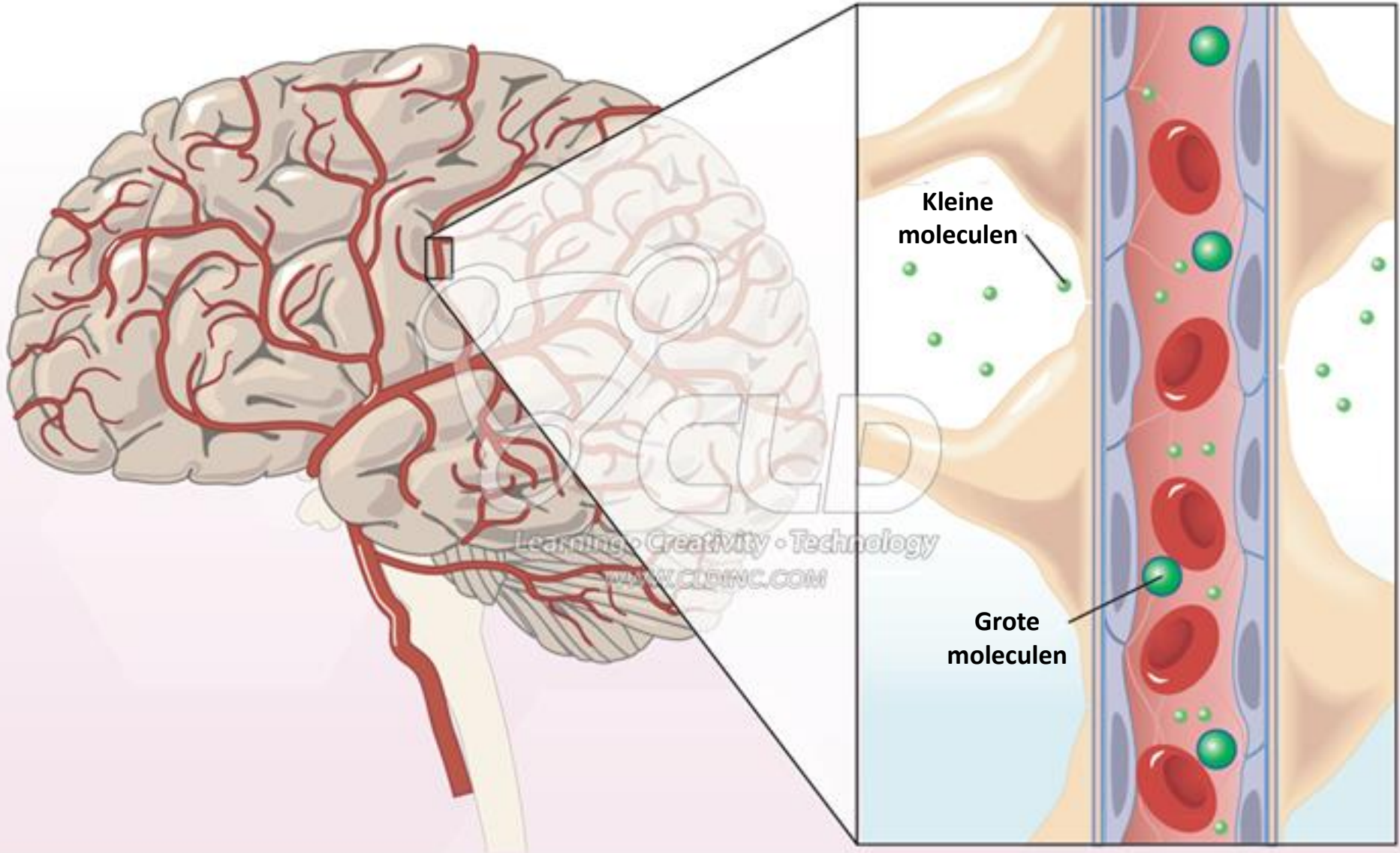
Catherine S Grasso<sup>1,24</sup>, Yujie Tang<sup>2-5,23,24</sup>, Nathalie Truffaux<sup>6,24</sup>, Noah E Berlow<sup>7</sup>, Lining Liu<sup>2-5</sup>, Marie-Anne Debily<sup>6,8</sup>, Michael J Quist<sup>1</sup>, Lara E Davis<sup>9</sup>, Elaine C Huang<sup>9</sup>, Pamelyn J Woo<sup>2-5</sup>, Anitha Ponnuswami<sup>2-5</sup>, Spenser Chen<sup>2-5</sup>, Tessa B Johung<sup>2-5</sup>, Wenchao Sun<sup>2</sup>, Mari Kogiso<sup>10</sup>, Yuchen Du<sup>10</sup>, Lin Qi<sup>10</sup>, Yulun Huang<sup>10,23</sup>, Marianne Hütt-Cabezas<sup>11,12</sup>, Katherine E Warren<sup>13</sup>, Ludivine Le Dret<sup>6</sup>, Paul S Meltzer<sup>13</sup>, Hua Mao<sup>10</sup>, Martha Quezado<sup>13</sup>, Dannis G van Vuurden<sup>14,15</sup>, Jinu Abraham<sup>9</sup>, Maryam Fouladi<sup>16</sup>, Matthew N Svalina<sup>1,17</sup>, Nicholas Wang<sup>1</sup>, Cynthia Hawkins<sup>18,19</sup>, Javad Nazarian<sup>20</sup>, Marta M Alonso<sup>21</sup>, Eric H Raabe<sup>11,12</sup>, Esther Hulleman<sup>14,15</sup>, Paul T Spellman<sup>1</sup>, Xiao-Nan Li<sup>10</sup>, Charles Keller<sup>9,17,25</sup>, Ranadip Pal<sup>7,25</sup>, Jacques Grill<sup>6,22,25</sup> & Michelle Monje<sup>2-5,25</sup>



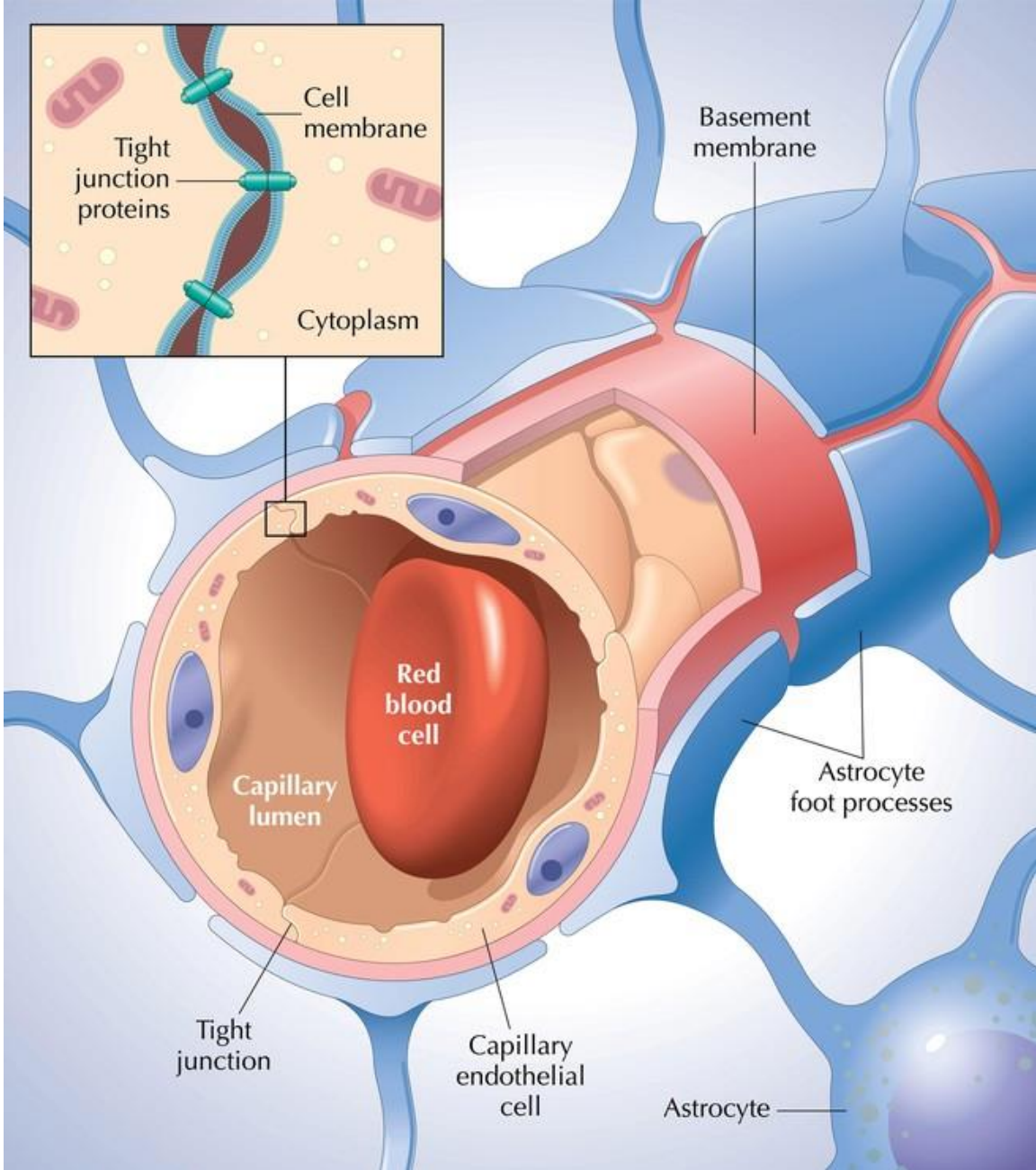
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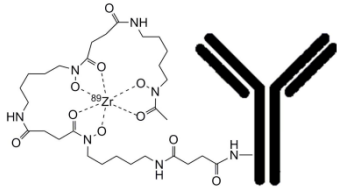


# Probleem = bloed-hersen-barrière









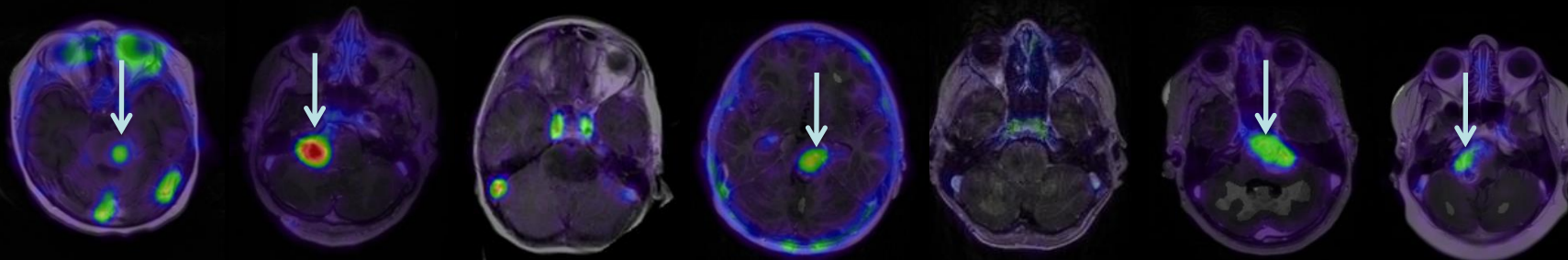
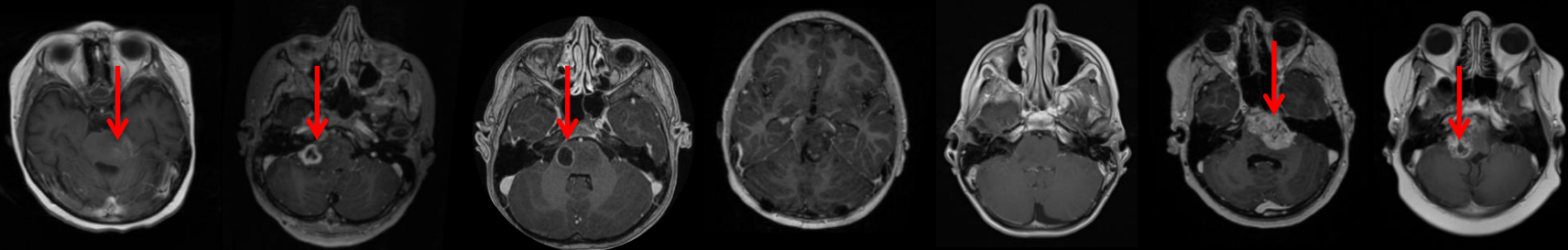
# Medicijnen zichtbaar maken

Labeled drug

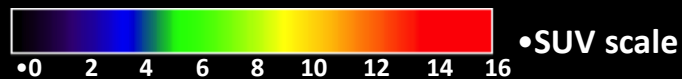


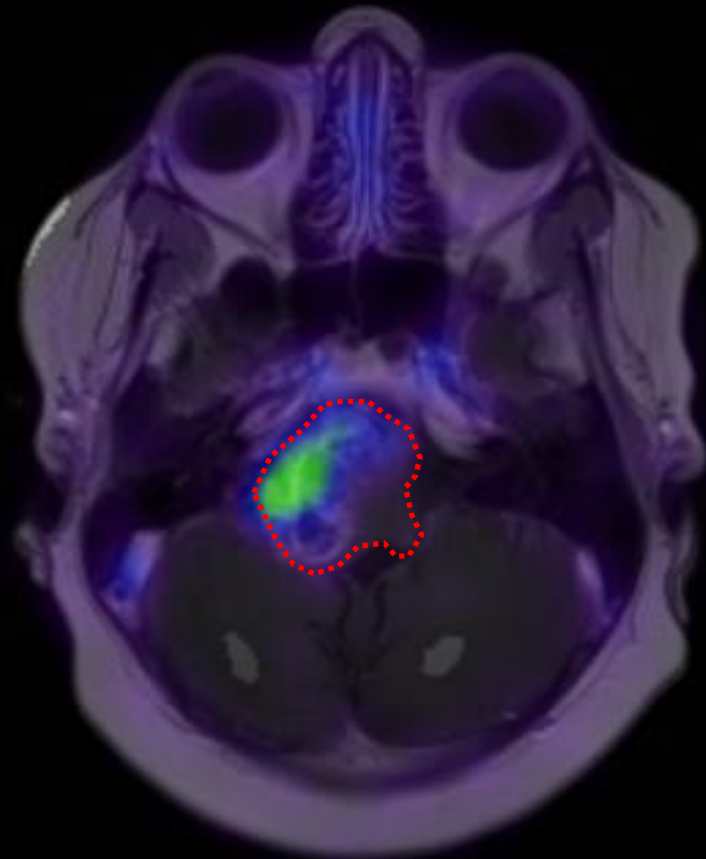
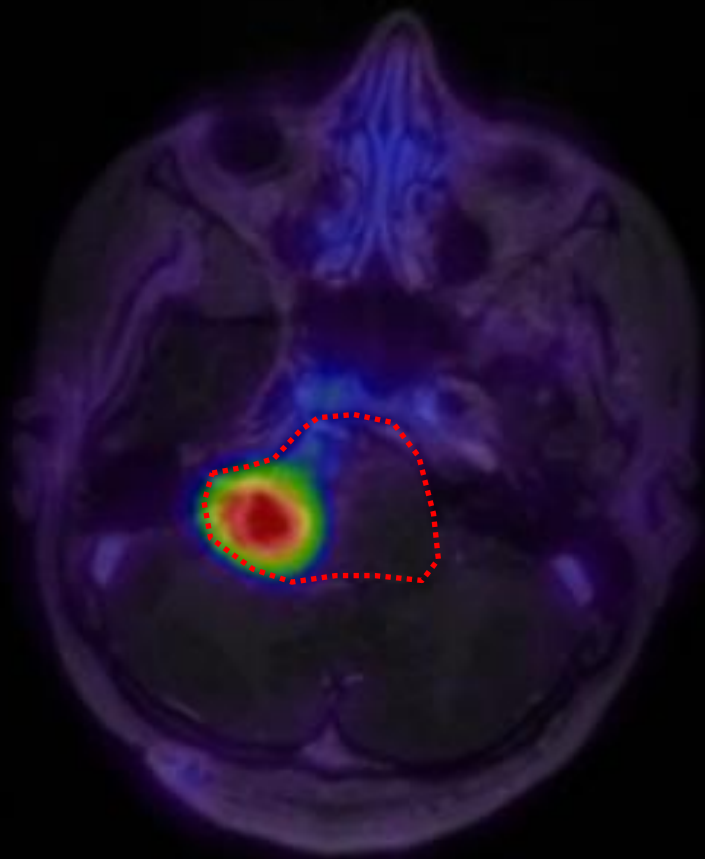
• Total dose: 0.9 MBq/kg (expected radiation dose of 20-45 mSv) + 3mSv (low dose CT) = 0.023 – 0.048 Gy

•MRI T1-weighed post- gadolinium



•PET-MRI fused

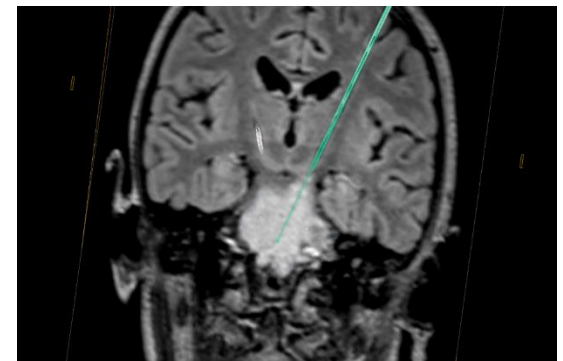
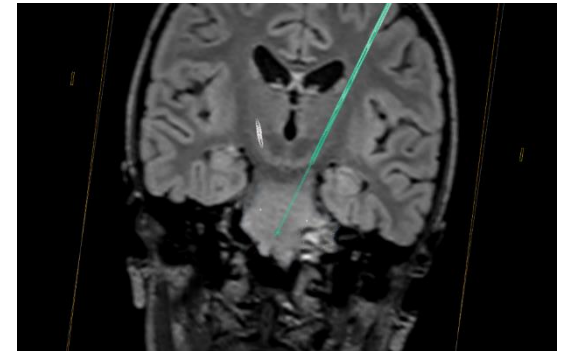




# Hoe krijgen we medicijnen beter over de bloed-hersenenbarrière?

## Speerpunt van Research in Het Máxima

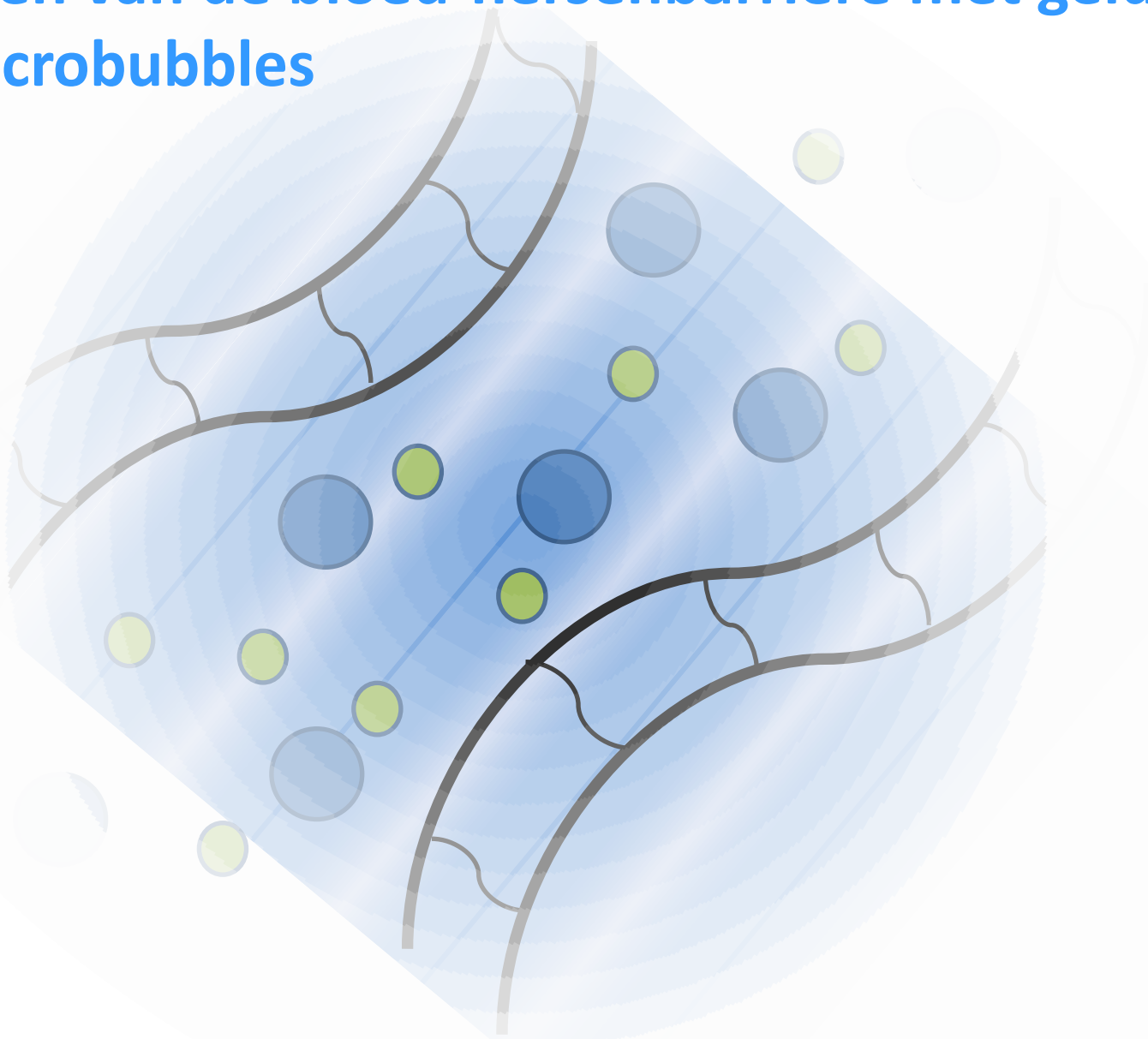
# Catheters – convection-enhanced delivery



# Iedere 4 weken chemotherapie rechtstreeks in de hersenstam

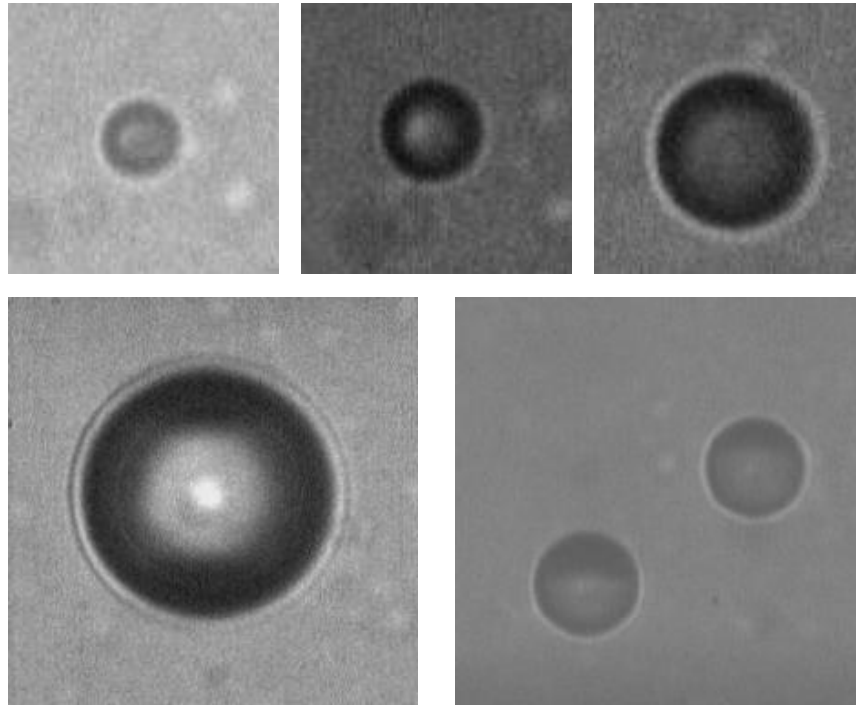


# Openen van de bloed-hersenenbarrière met geluid en microbubbles



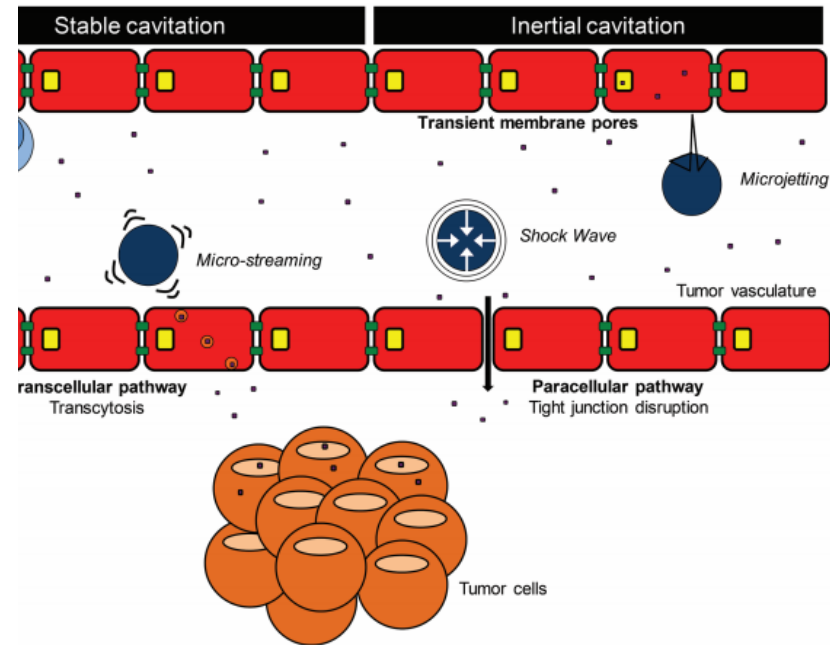
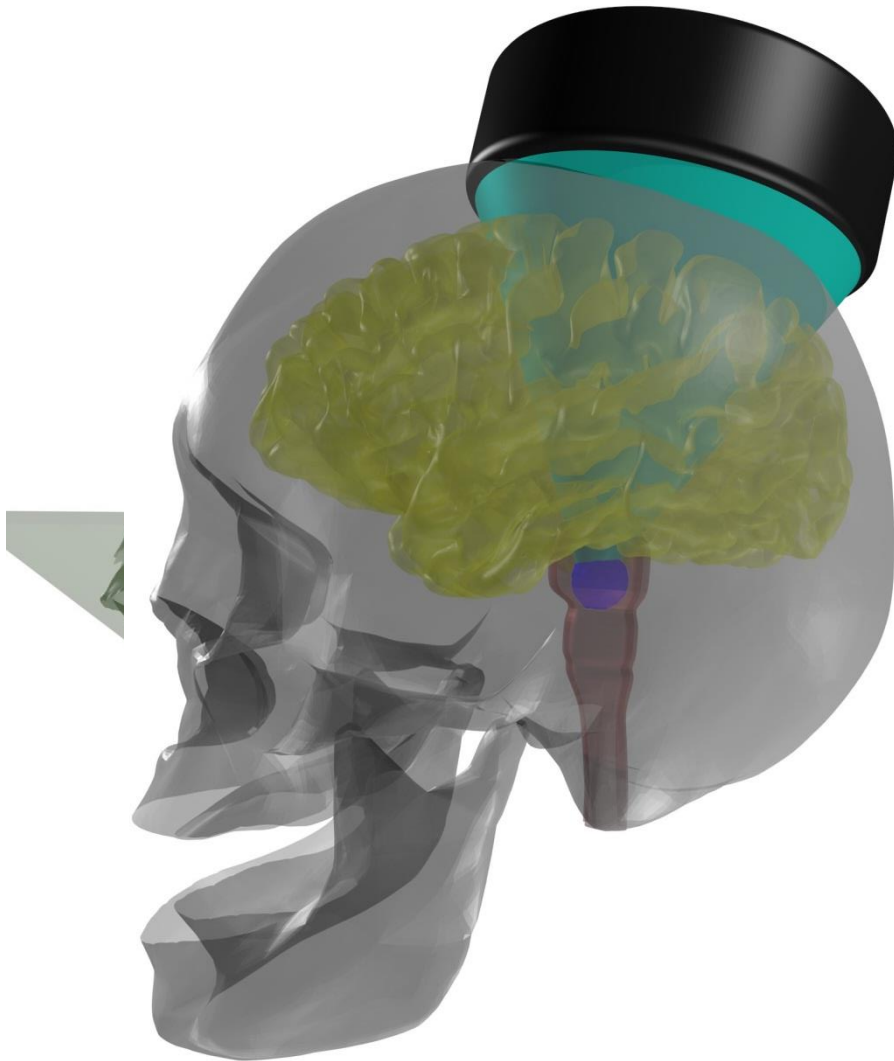
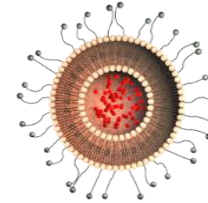


# Trillende microbubbles



*Faez, Skachkov et al., UMB, 2012*

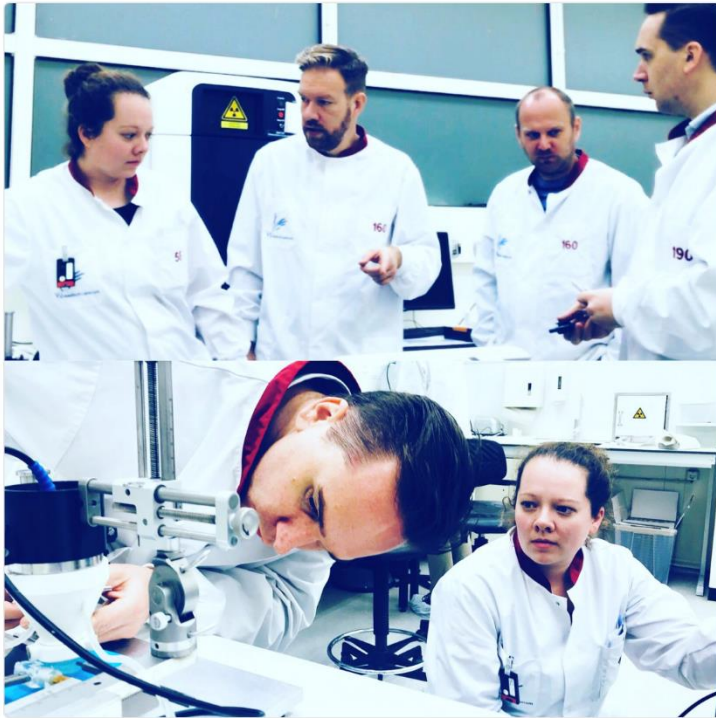
# Laboratoriumonderzoek in voorbereiding voor behandelstudie





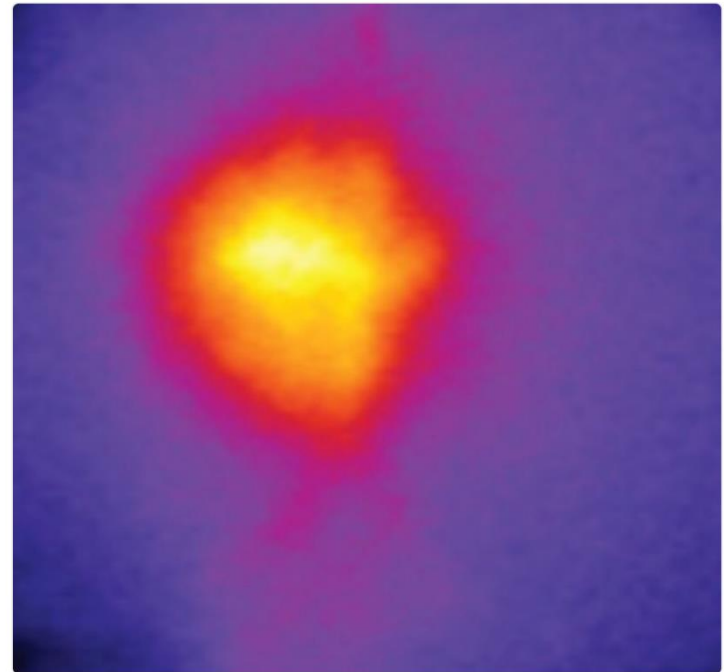
**Dr Dannis v. Vuurden**  
@DannisVV

Investigating how to treat brain tumors using #soundwaves! #research in the #laboratory @VUmcAmsterdam funded by @kwf\_nl and @NWO\_TTW #ultrasound #hifu

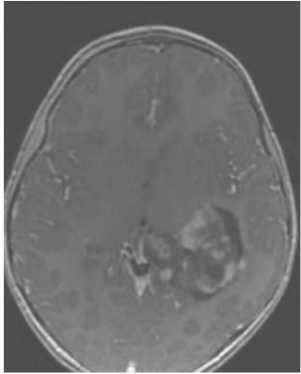


**Dr Dannis v. Vuurden**  
@DannisVV

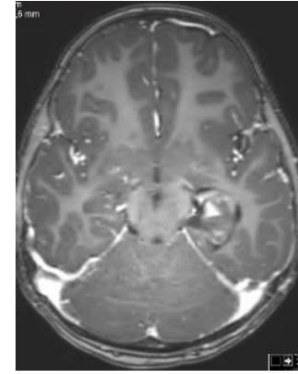
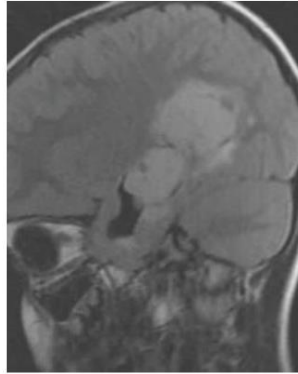
Successful #experiment studying #sound for better #braintumor #treatment #hifu #dipg #research funded by @kwf\_nl and @NWO\_TTW



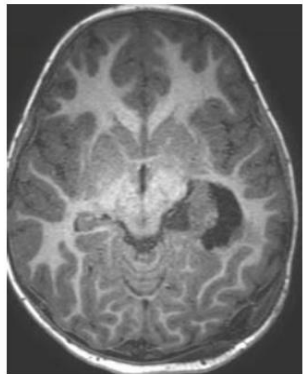
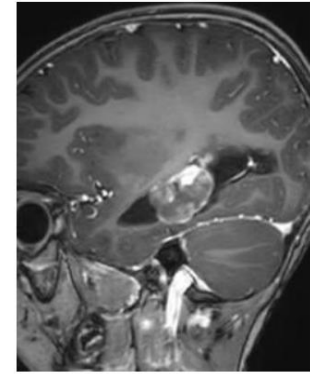
# Zorginnovatie – intra-operatieve MRI



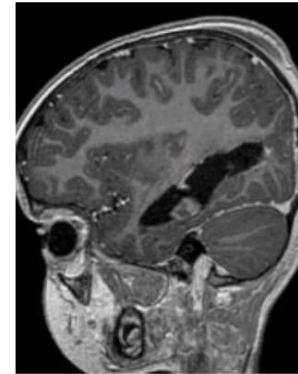
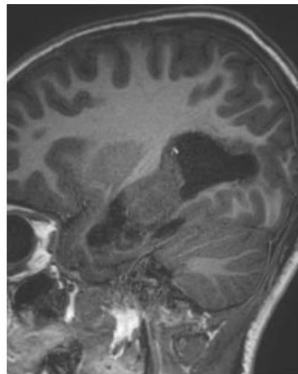
A. Patiënt geb. 2012



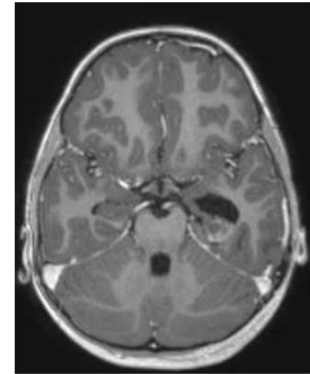
C. Progressie restant tumor



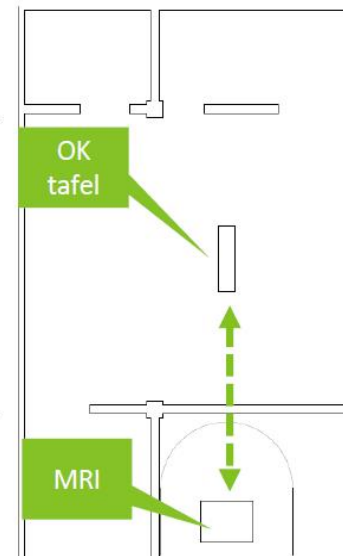
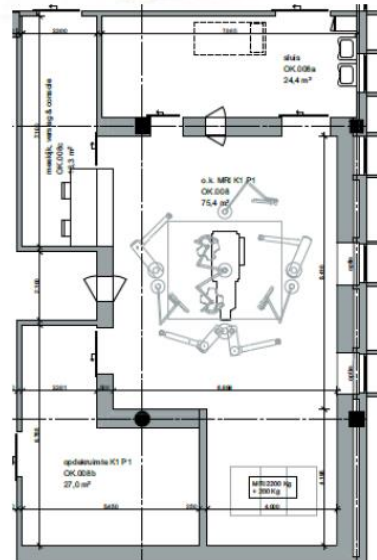
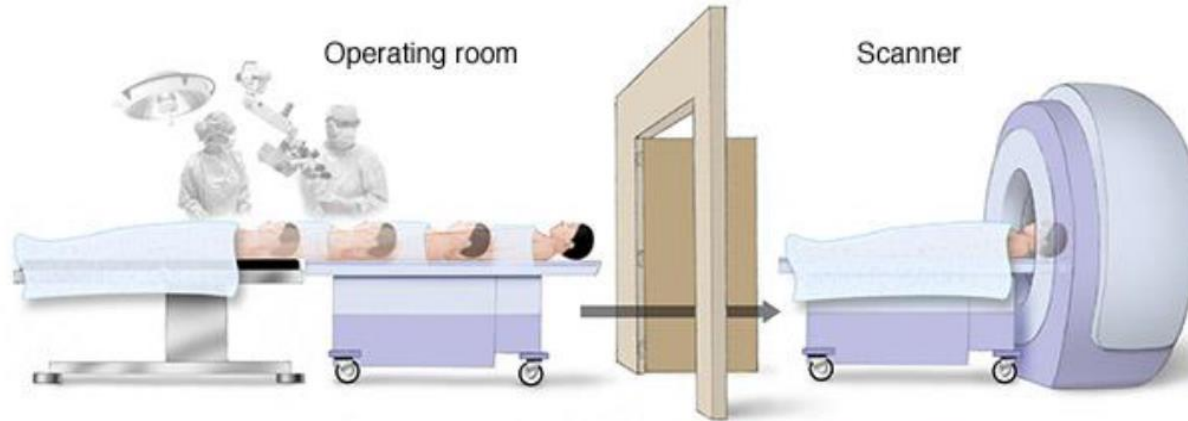
B. Laaggradig astrocytoom; partiele resectie



D. Aanvullende resectie



# Zorginnovatie – intra-operatieve MRI



# Zorginnovatie – intra-operatieve MRI



# Hersentumoren bij kinderen

Betere behandeling door innovatie in research en zorg

- Unieke, zeldzame vormen van kanker op de kinderleeftijd
- Hoge sterfte
- Ernstige lange termijn-effecten
- Matige kwaliteit van leven
- Concentratie van zorg en translationele research essentieel
- Innovatieve research en zorginnovatie
- Samenbrengen van top kennis en expertise
- Doel: betere overleving met goede kwaliteit van leven

