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Brain Metastases Management for Palliative Care SpRs

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Contents

- An overview of brain metastases from a Clinical Oncologist point of view
  - Background
  - Initial management
  - Further management options
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- Case studies

Background on Brain Mets

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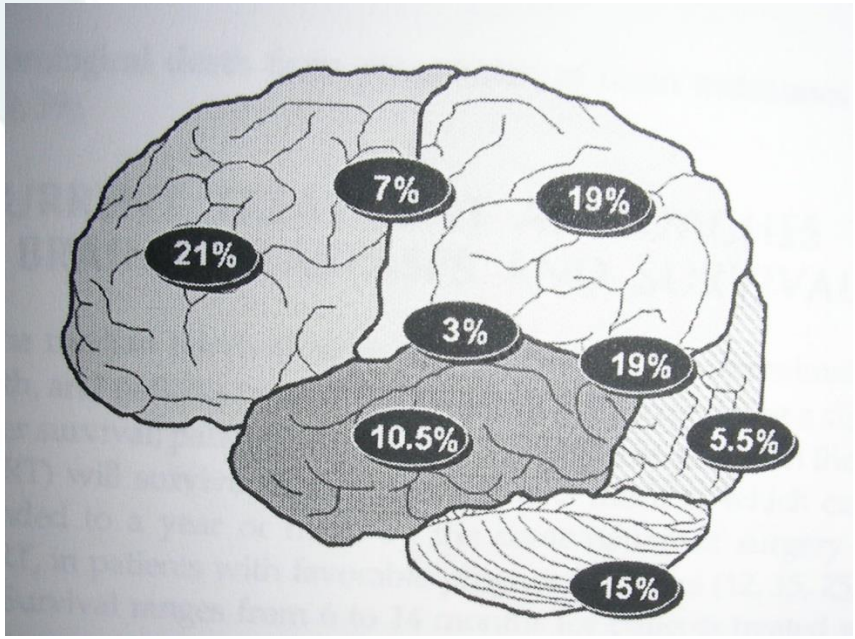
- True incidence not known
- Estimated 16000 cases per year in UK
- Estimated 20 to 40% pts develop mets during course of cancer
- Most pts are symptomatic
- Increase due to better systemic therapy (=longer survival) and improved imaging
- Most common primary sites are breast, lung, melanoma and renal

Presenting symptoms

- Headache 49%
- Focal weakness 30%
- Mental disturbances 32%
- Ataxia 21%
- Seizures 18%
- Speech difficulty 12%
- Visual disturbance 6%
- Sensory disturbance 6%
- Limb ataxia 6%

Locations of metastases

- Commonly located in gray-white matter junction and superficial arterial fields
- Distribution reflects blood flow
- 85% in cerebral hemispheres
- 10 to 15% in cerebellum
- 1 to 3 % in brain stem
- Pelvic and GI localise to posterior fossa



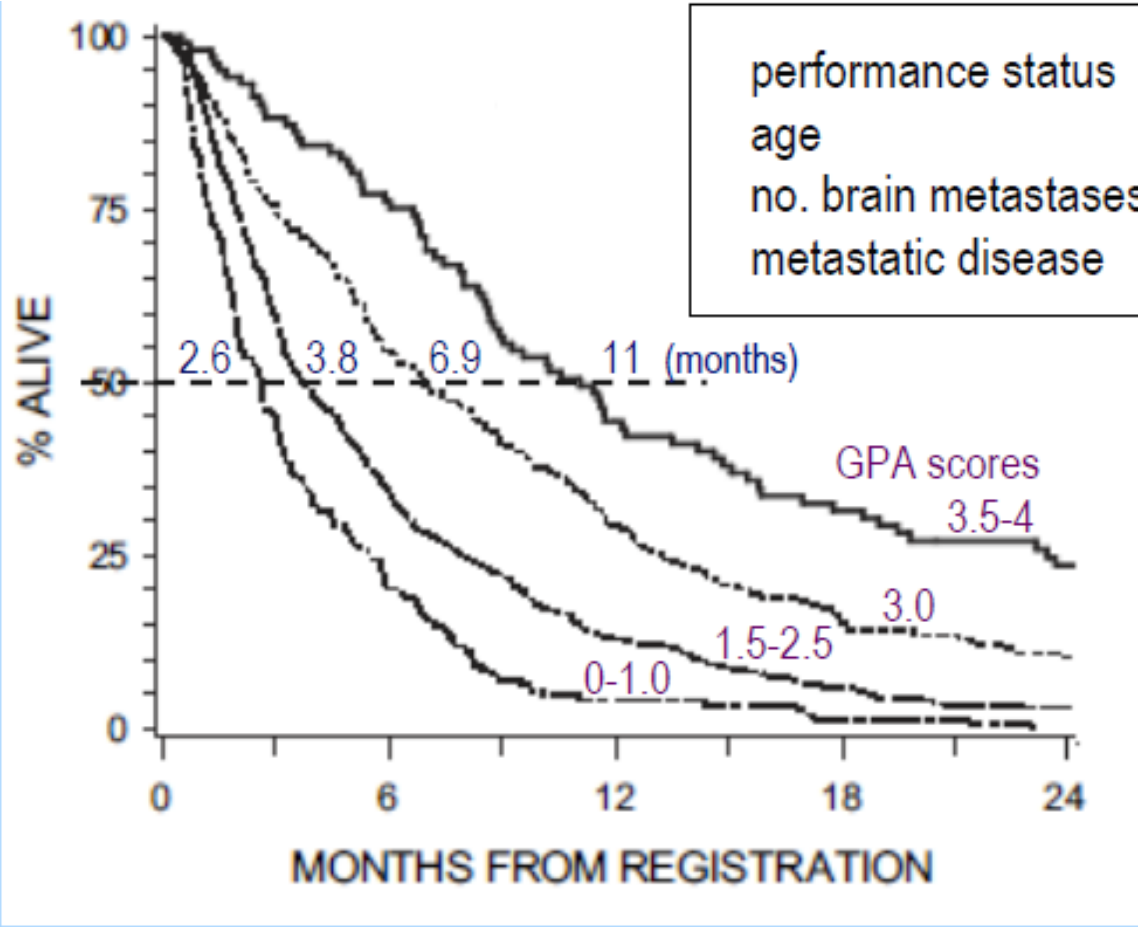
Prognosis

- Difficult to be exact
- Historically very poor: 8 – 12 weeks
- Increasing now however
  - Earlier detection
  - Better local and systemic treatments
  - Median 7 months for all comers
  - Some considerably longer e.g. HER2 +ve breast

Prognostic factors

- Depends on primary tumour site
- Graded Prognostic Assessment (GPA)
    - Performance status
    - Number of brain mets
    - Histological subtype
    - Age
    - Presence of extra cranial mets
- Recursive Partitioning Analysis (RPA)

Prognosis by GPA class

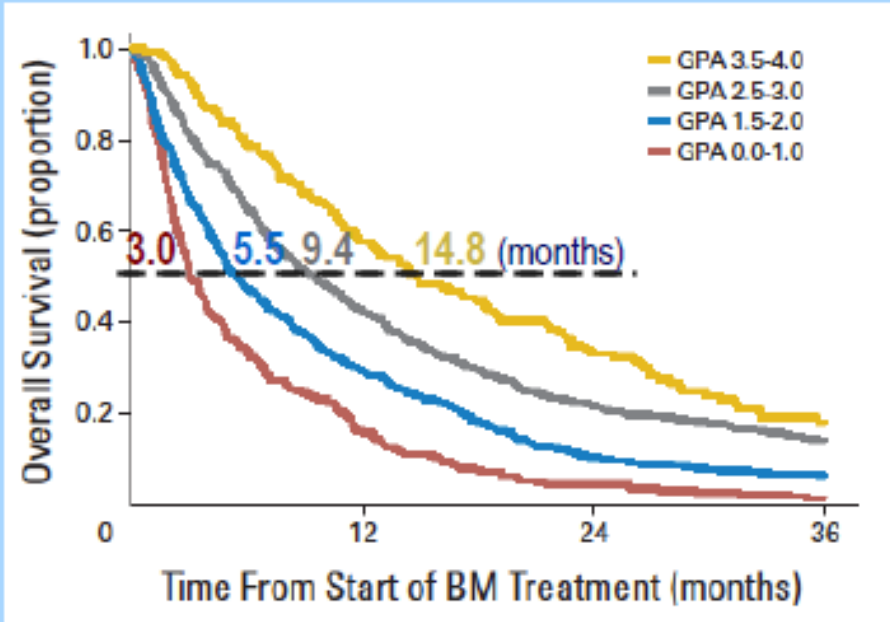


Median survival: tumour site[1]

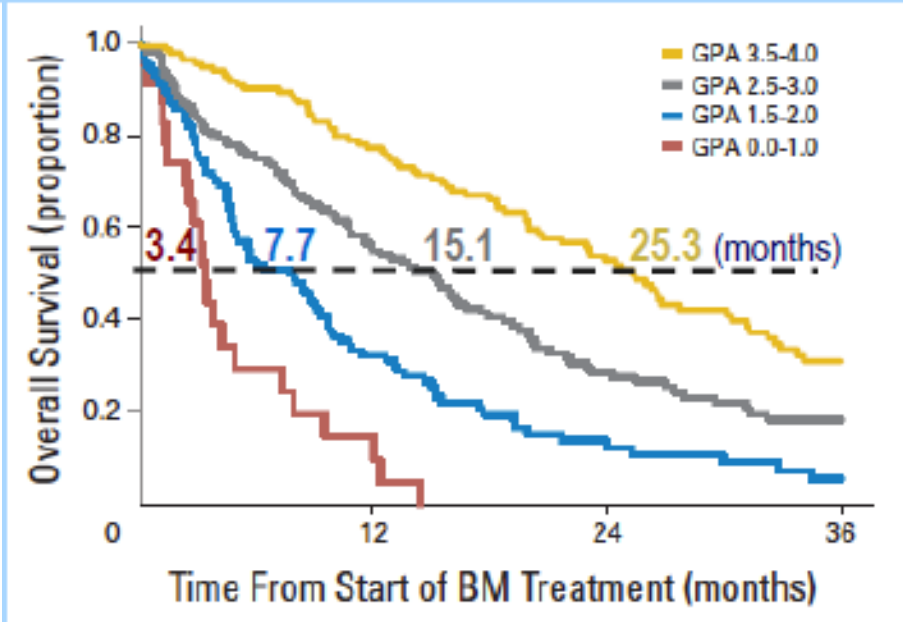
- Breast – 13 months [3 – 25]
- NSCLC – 7 months [3 – 14]
- SCLC – 5 months [2 – 17]
- Melanoma – 6 months [3 – 13]
- Renal cell – 9 months [3 – 14]
- GI – 5 months [3 – 13]

Prognosis by tumour/GPA

NSCLC – GPA classes



Breast cancer



Investigations

- If you suspect brain metastases please do an MRI head with contrast
- No point in a CT head
  - Cannot exclude mets, is not good enough quality to identify all mets, we will always ask for an MRI
- Urgency depends on symptoms

Initial management

- Depends on the symptoms and scan appearances
  - Steroids?
    - Dexamethasone
  - Anti-epileptics?
    - Phenytoin, levetiracetam, sodium valproate
  - Best supportive care?
    - Includes the above
  - Explanation to patient and family

Steroids – friend or foe?!?

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- Appropriate use of steroids is hugely important!
- Controls oedema related symptoms
  - Headache, nausea, vomiting
  - Radiotherapy induced inflammation
- Is NOT a treatment for seizures
- Brain METS do NOT need massive doses (unlike primary brain tumours)
  - 4mg once daily is usually enough, BD if significant oedema, not higher than that unless advised by us or neurosurgeons
- Can have significant side effects
- Aim to wean down to the lowest dose which controls symptoms

Decision Making

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- Need to take into account
  - Patient factors
    - Symptoms
    - Wishes
    - Comorbidities
    - Performance status
  - Tumour factors
    - Location
    - Size/total volume
    - Extra-cranial disease
    - Prognosis

Further management

- There are always options
  - Whole brain radiotherapy (WBRT)
  - Stereotactic radiosurgery/therapy (SRS/SRT)
  - Surgical resection +/- cavity SRT
  - Systemic treatment
  - Best Supportive Care
- Refer to the Neuro-oncology specialist MDT
  - On a Thursday @ 12:30, deadline Tuesday @ 3pm
  - Need as much info as possible

Surgical resection

- I am not a surgeon!
- Good option
  - Oedema
  - Solitary/oligometastases with controlled extracranial disease
  - Location not likely to leave neurological deficit
- Bad option
  - Poor PS
  - Multiple metastases
  - Location likely to leave neurological deficit
  - Widespread/ progressing extracranial disease

Radiotherapy options

- Cavity SRT
  - Post resection of solitary/few mets
- SRS
  - Solitary/few small mets
- SRT
  - Solitary/few larger mets
- WBRT
  - Multiple/massive mets

Firstly…what is radiotherapy?

- Very briefly…
  - Very strong x rays
  - Highly targeted at the area we shine it at!
  - Kills cancer cells and normal tissue
  - Need to balance these – the therapeutic ratio
  - The idea of fractionation is allows normal tissue to recover but not cancer cells – increases the therapeutic ratio
  - Side effects mostly from normal tissue irradiation
  - We call each treatment a fraction (#)

Whole Brain Radiotherapy

- Traditionally the way to treat brain metastases
- Quick to arrange
- Mask and planning CT
- Draw a box around the whole head, 2 parallel fields, one either side of the head and zap
  - I promise it is more complex than that really!
- 5 or 10 fractions
- Can be given at CCC-W or CCC-A
- Benefits
  - Treats the whole brain (obviously…!)
- Disadvantages
  - Treats the whole brain!! Side effects!

Whole brain Radiotherapy

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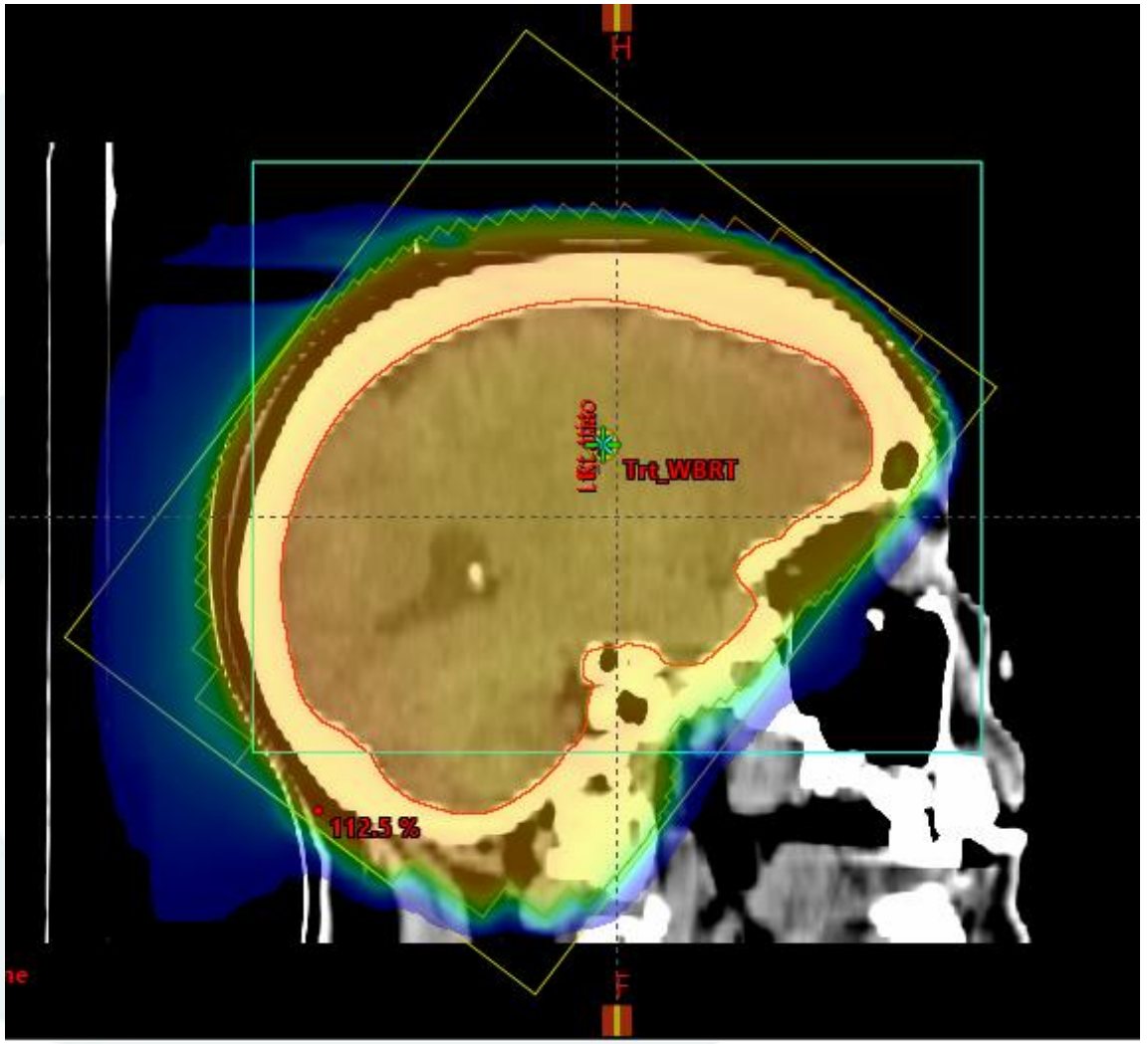

Whole brain Radiotherapy

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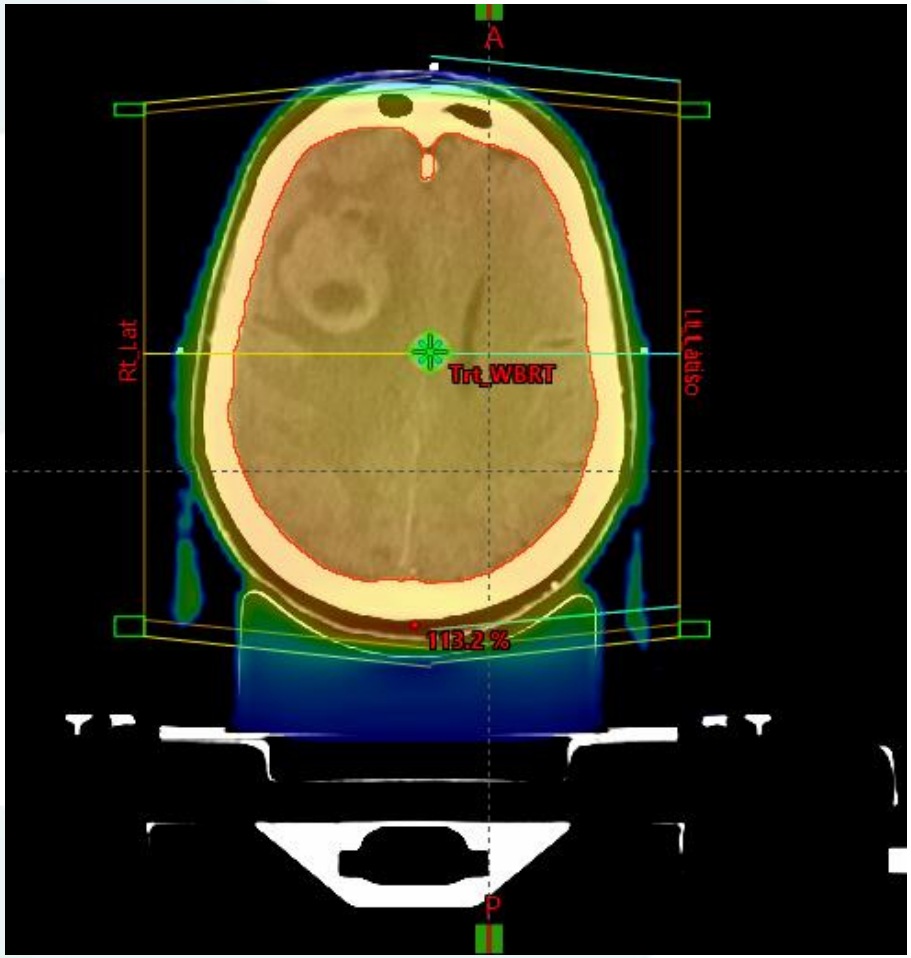

Acute and Late Toxicities of Brain RTx

- Acute
  - Fatigue
  - Alopecia
  - Nausea
  - Headaches
- Late
  - Somnolence (ranging from mild to extreme)
  - Short term memory impairment
  - Concentration impairment
  - Alopecia can be permanent
  - Radionecrosis

Quick update on HS-WBRT

- The hippocampus
  - Allows consolidation of new memories into long term memory
  - Irradiated in WBRT
  - Starting to become practice to do hippocampal sparing in select patients
    - Takes a lot of time to outline
    - Increase in treatment time on the bed
    - Risk of under-dosing
    - However – evidence of benefit/need is increasing

Stereotactic RadioSurgery

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- A single (longer) fraction
- Size/volume limited for safety
- Longer to arrange, treated on Thursdays only
- Treated only at CCC-A (at the moment)
- We use a Linear Accelerator (Linac)
  - Other machines are available (Gamma Knife®/Cyber Knife®)
  - All perform essentially the same role
- Need a mask, planning CT and planning MRI
- Highly, highly targeted (2mm margin)

Stereotactic RadioSurgery

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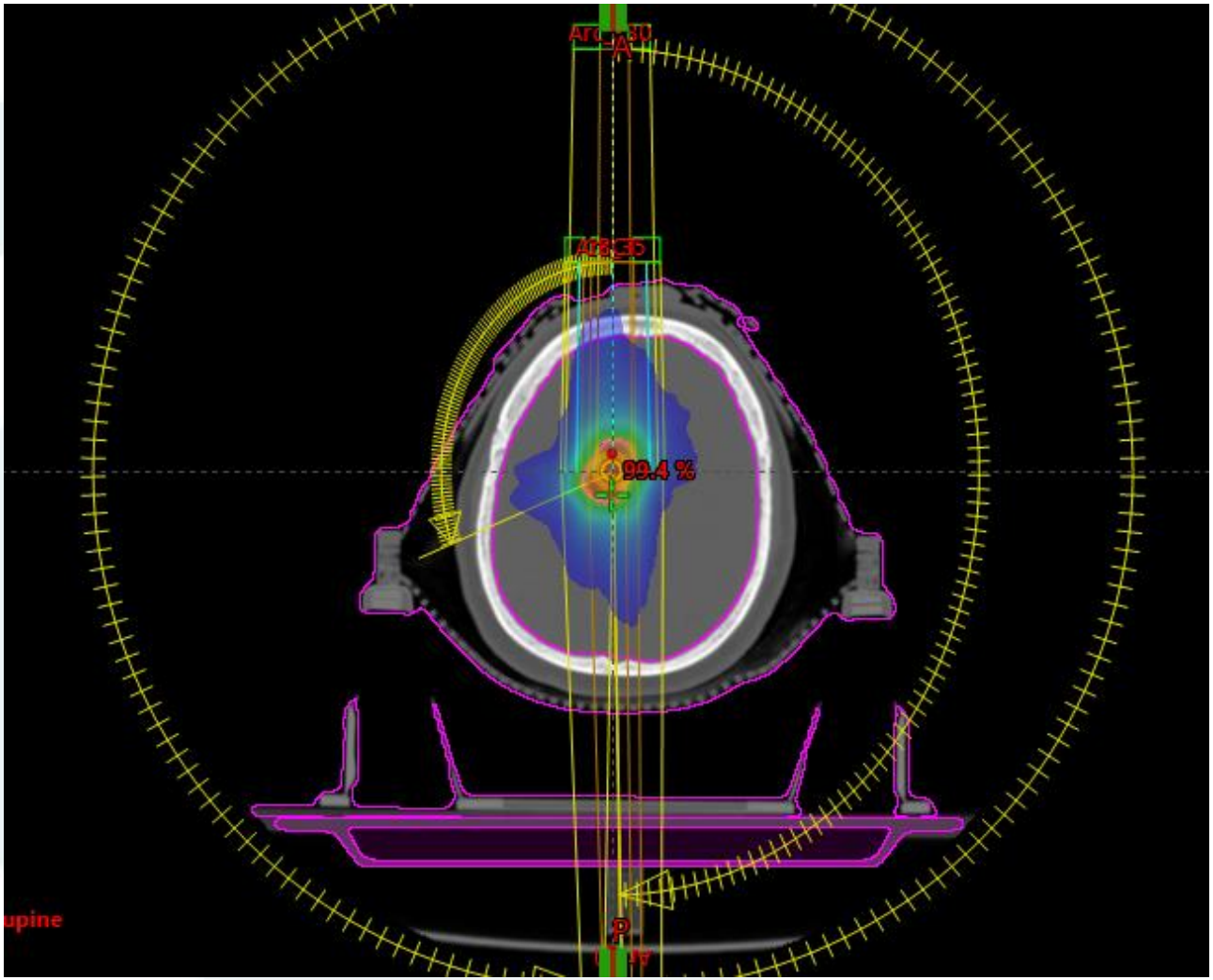

Stereotactic RTx/Cavity SRT

- 5 fractions
- Can be given at CCC-W or CCC-A
- Mask and planning CT
- Highly targeted (2mm margin)
- Given over more fractions to spare normal tissue for larger lesions

Stereotactic RTx/Cavity SRT

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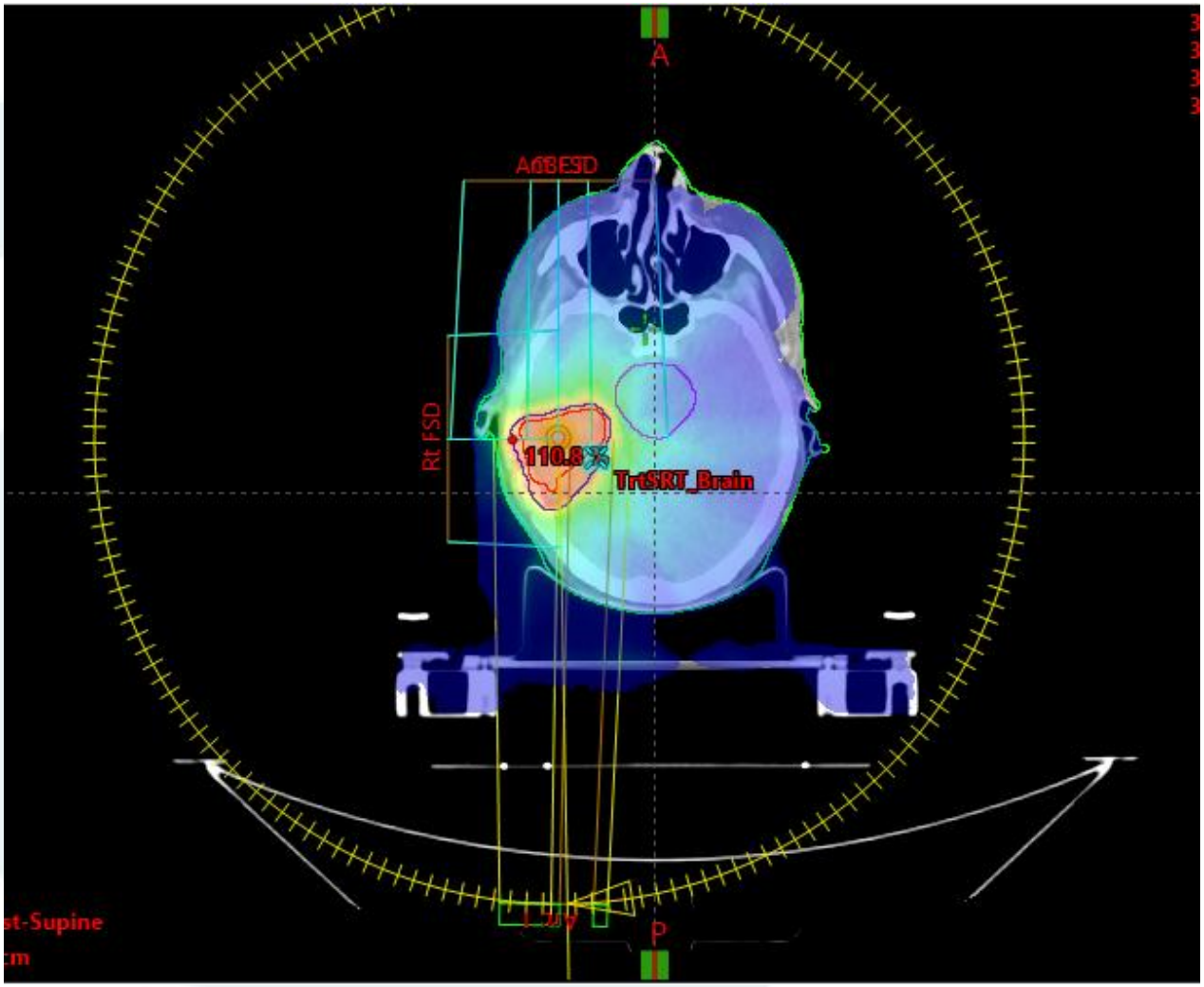

Post RTx Management

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- For SRS they need fairly high dose Dex around treatment day
  - 8mg day -1, 0, 1, 2
- Otherwise manage their dex to wean down to the lowest dose which controls symptoms
- Drop by half every 3 days is a rough guide
- Palliative care referral generally sensible as mostly the prognosis is not as good as before brain mets were diagnosed

Follow up

- Depends on the oncologist
  - Some neuro-oncologists will keep looking after them, some will discharge back to primary oncologist
- MRI
  - 6 – 8 weeks post RTx
  - 3 monthly thereafter
- Systemic treatment done by primary oncologist
- Treat further lesions as they appear
  - Further SRS if solitary/oligo vs WBRT
  - Start the whole process from the beginning

Leptomeningeal disease (LMD)

- What is it?
- Who has it?
- Presentation?
- Management?
- Prognosis?

LMD: What is it?

- Cancer spreads through CSF/meninges
  - In brain or spine
- Classical LMD
- Nodular LMD
- Incidence 5 – 10%

LMD: who has it?

- Typically
  - Breast
  - Lung
  - Melanoma
  - Others of course possible
- Seems to also be appearing post radiotherapy
  - ?breaking down the BBB
  - ?patients living longer to develop it

LMD: Presentation

- Symptoms
  - Seizures
  - Nerve palsies
  - Anything neuro
  - Incidental/asymptomatic
- Investigation
  - MRI head with contrast
  - MRI spine with contrast
  - LP for CSF cytology if needed to confirm

LMD: Management

- Localised treatment
  - Radiotherapy
  - WBRT only option for intracranial
  - Consider localised vs whole spine RTx for spine
- Systemic treatment
  - Chemotherapy
    - High dose intrathecal methotrexate/pemetrexed/capecitabine/temozolomide
  - Targeted treatments
    - Anti EGFR e.g. afatinib/ anti ALK e.g. crizotinib
- <u>Best supportive care</u>

LMD: Prognosis

- Poor ☹
- Median survival around 8 – 12 weeks….

Summary

- An overview of brain metastases from a Clinical Oncologist point of view
  - Background
  - Initial management
  - Further management options
  - WBRT/SRS/SRT details
  - Leptomeningeal disease
- Time for case studies!

Case Studies

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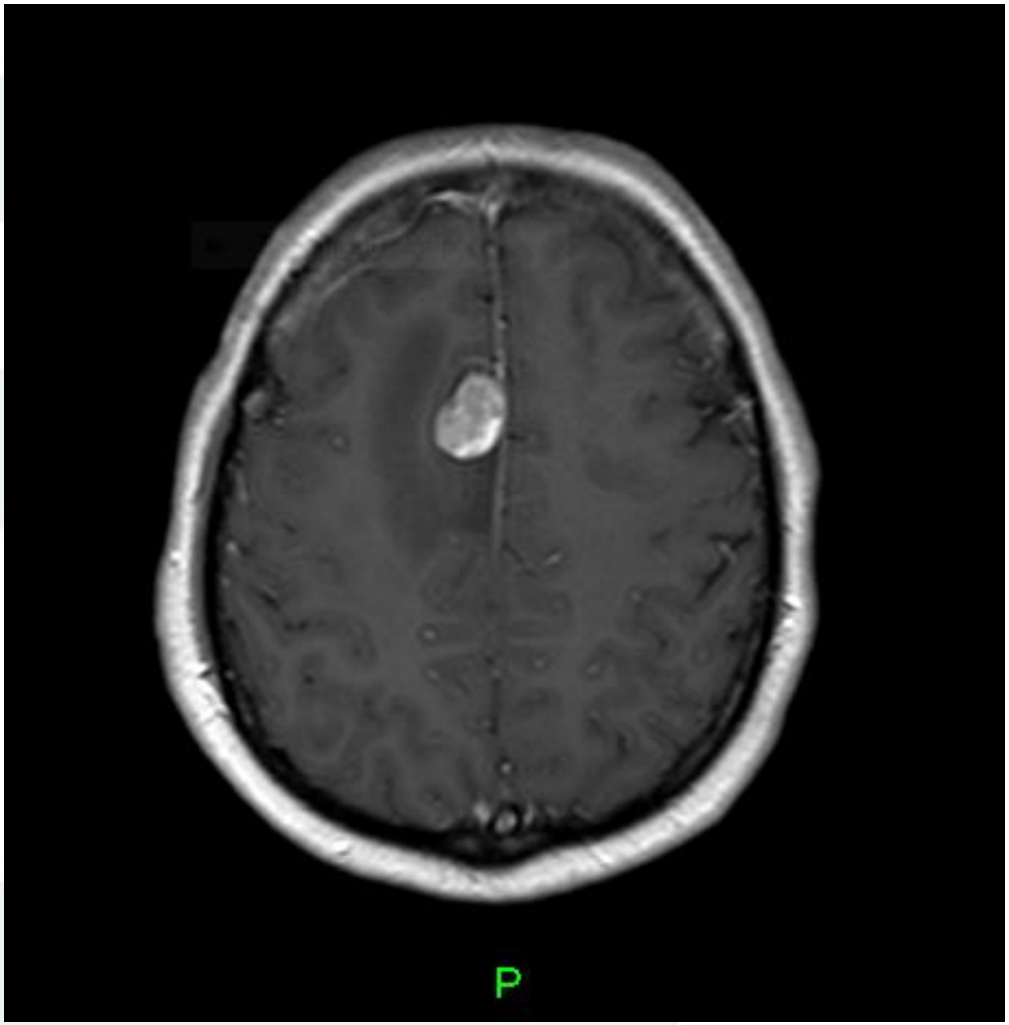
- Case 1 - melanoma
- Case 2 – renal cell carcinoma
- Case 3 – lung/renal cancer
- Case 4 – breast cancer meningeal disease
- Case 5 – melanoma mets and meningeal
- Case 6 – breast cancer

Case 1 A.S.

- 52y female
  - Previous melanoma resected from scalp 2018
  - Presented Oct 2019 with difficulty in concentrating, headaches, numbness in right fingers
  - MRI showed solitary right frontal parafalcine metastasis
  - Staging CT - no extra cranial disease
  - Not for surgery due to location
  - PS 0

Case 1 A.S.



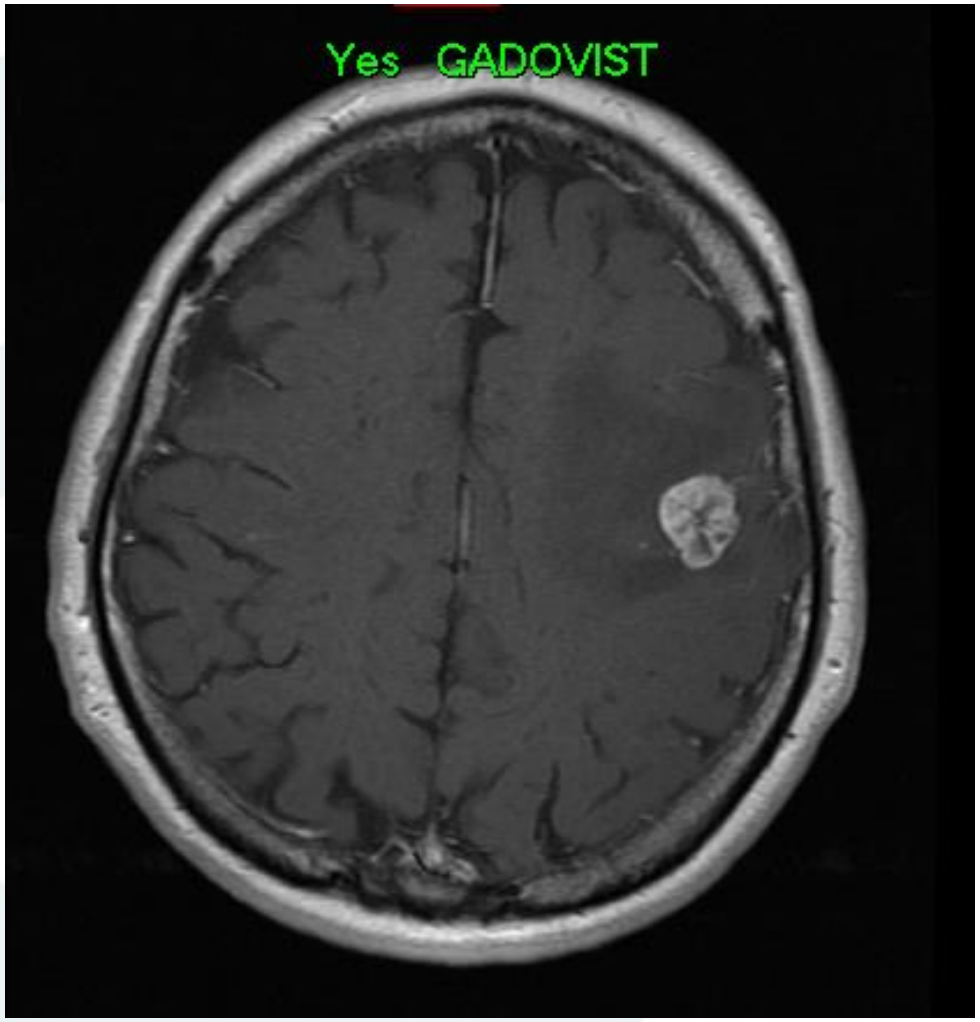
Case 1 A.S.

- She received SRS to this lesion last week
- She is due to see medical oncologist this week to discuss systemic treatment – likely immunotherapy
- Prognosis???

Case 2 E.W.

- 74y male
  - Diagnosed with RCC 2017
  - Received pazopanib then nivolumab
  - Stopped for toxicity
  - Presented Feb 2019 with slurred speech and right facial and hand weakness
  - MRI – solitary left frontal metastasis
  - Extracranial disease stable
  - Not for surgery due to location
  - PS 1

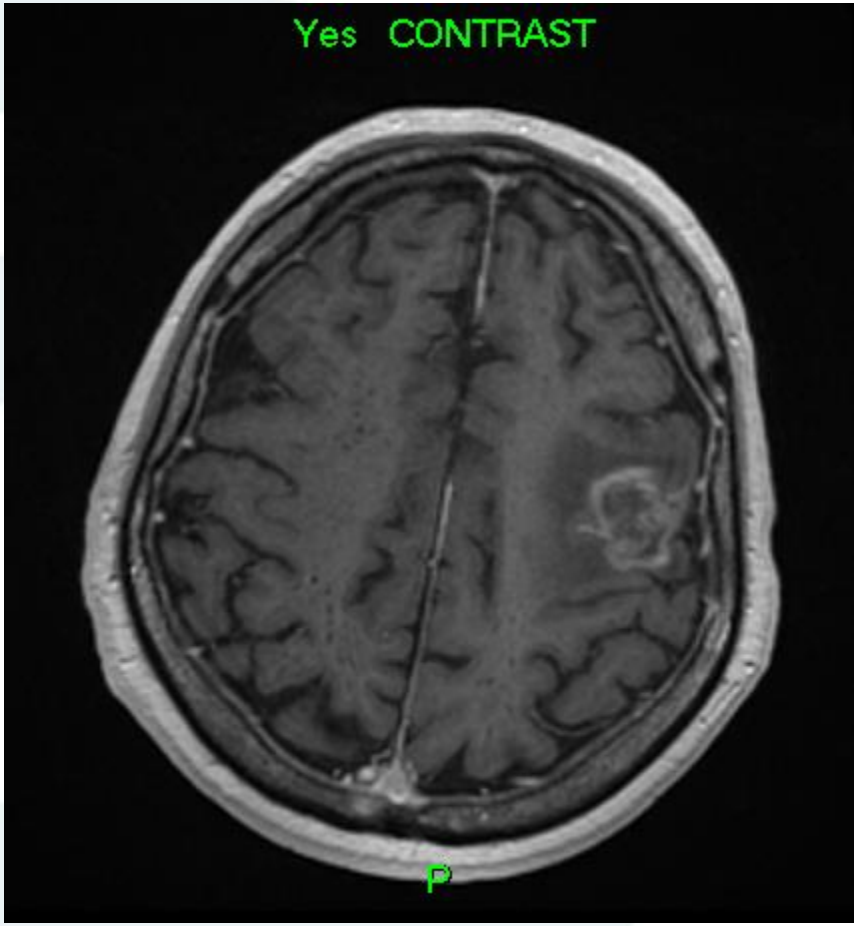
Case 2 E.W.



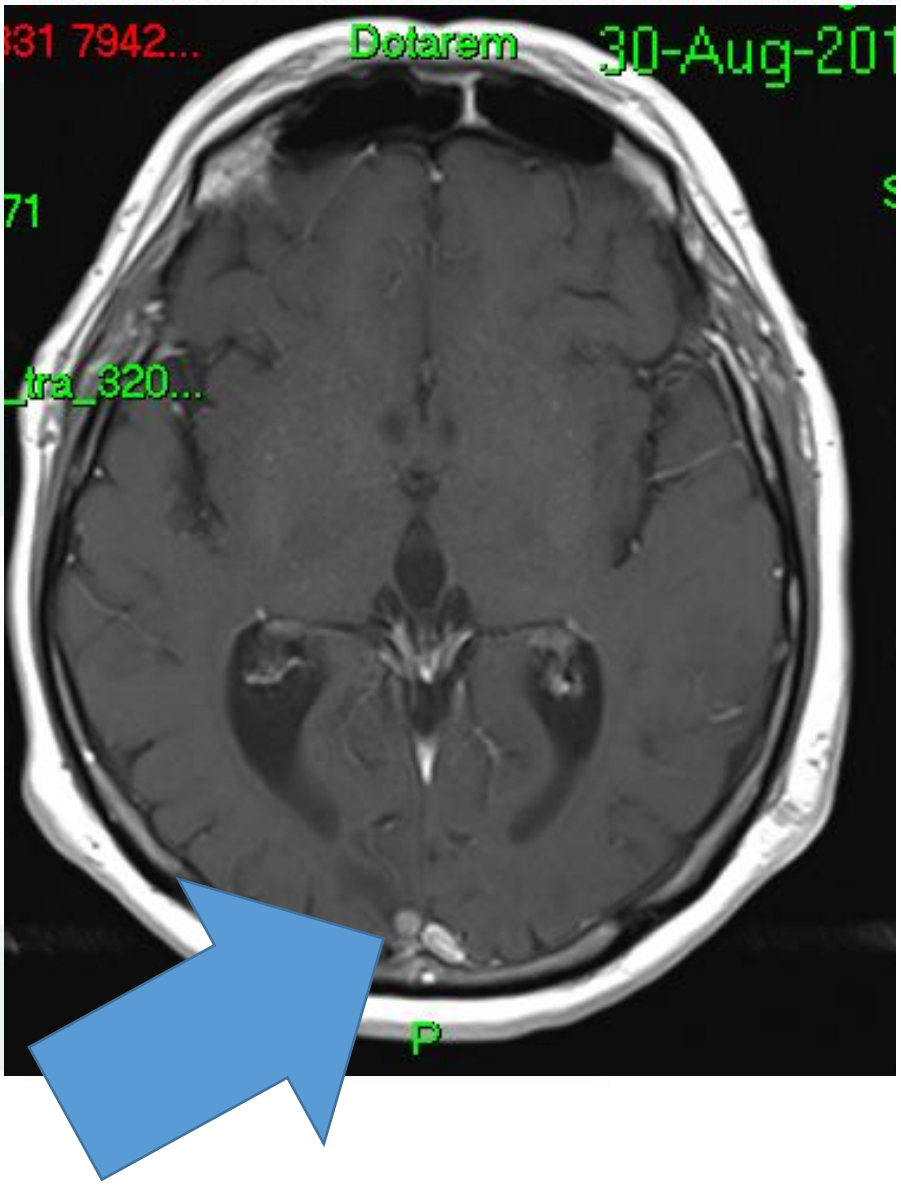
Case 2 E.W.

- He received SRS to this met in April 2019
- His post treatment scan showed some inflammation which was felt to be treatment related
- Had another MRI at 3 months

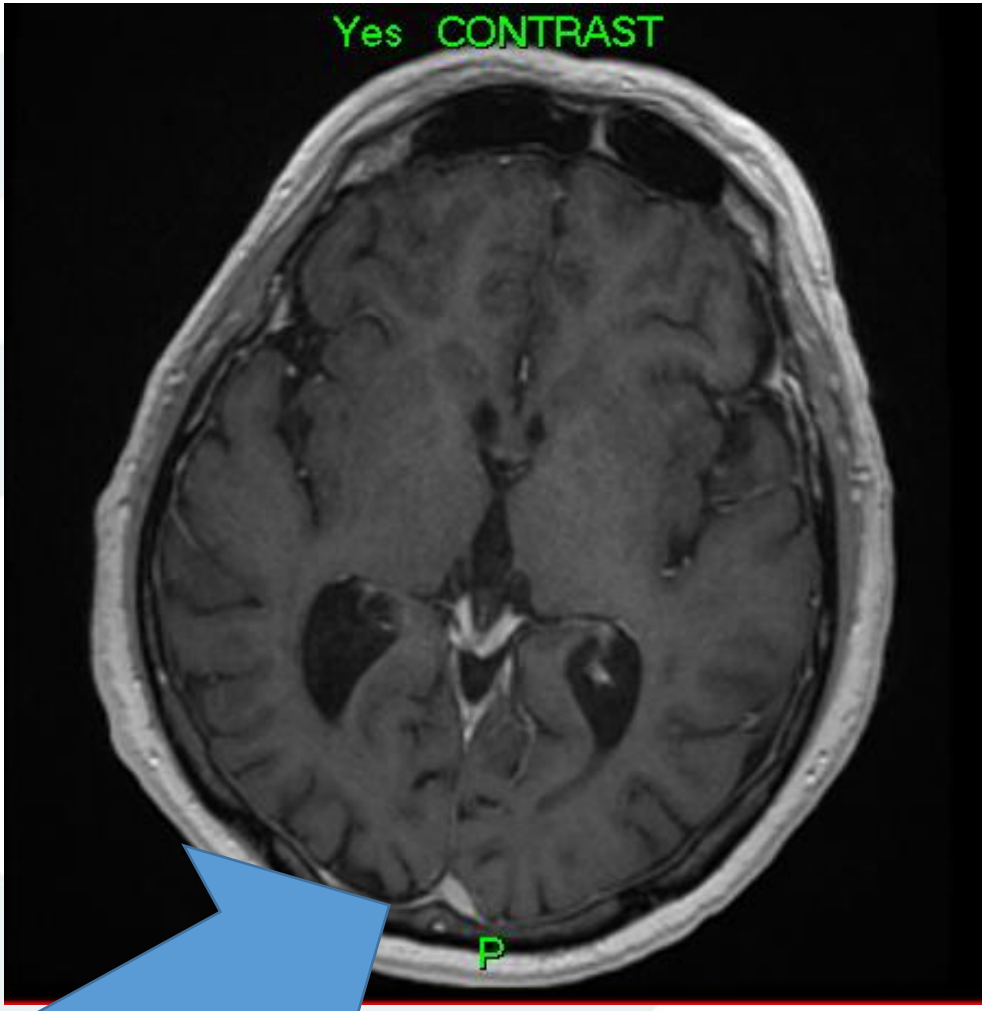
Case 2 E.W.



Case 2 E.W.



Case 2 E.W.



Case 2 E.W.

- He is currently fit and well with no major symptoms or side effects, but still on dexamethasone for oedema
- 10 months after his brain met diagnosis
- Third line systemic treatment (in total since 2017 diagnosis)

Case 3 A.H.

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- 65y male
  - April 2015 lobectomy for lung cancer
  - Nov 2015 nephrectomy for ?second primary RCC vs lung ca met
  - Oct 2016 had 2 seizures
  - MRI showed solitary right frontal lobe metastasis with significant oedema

Case 3 A.H.

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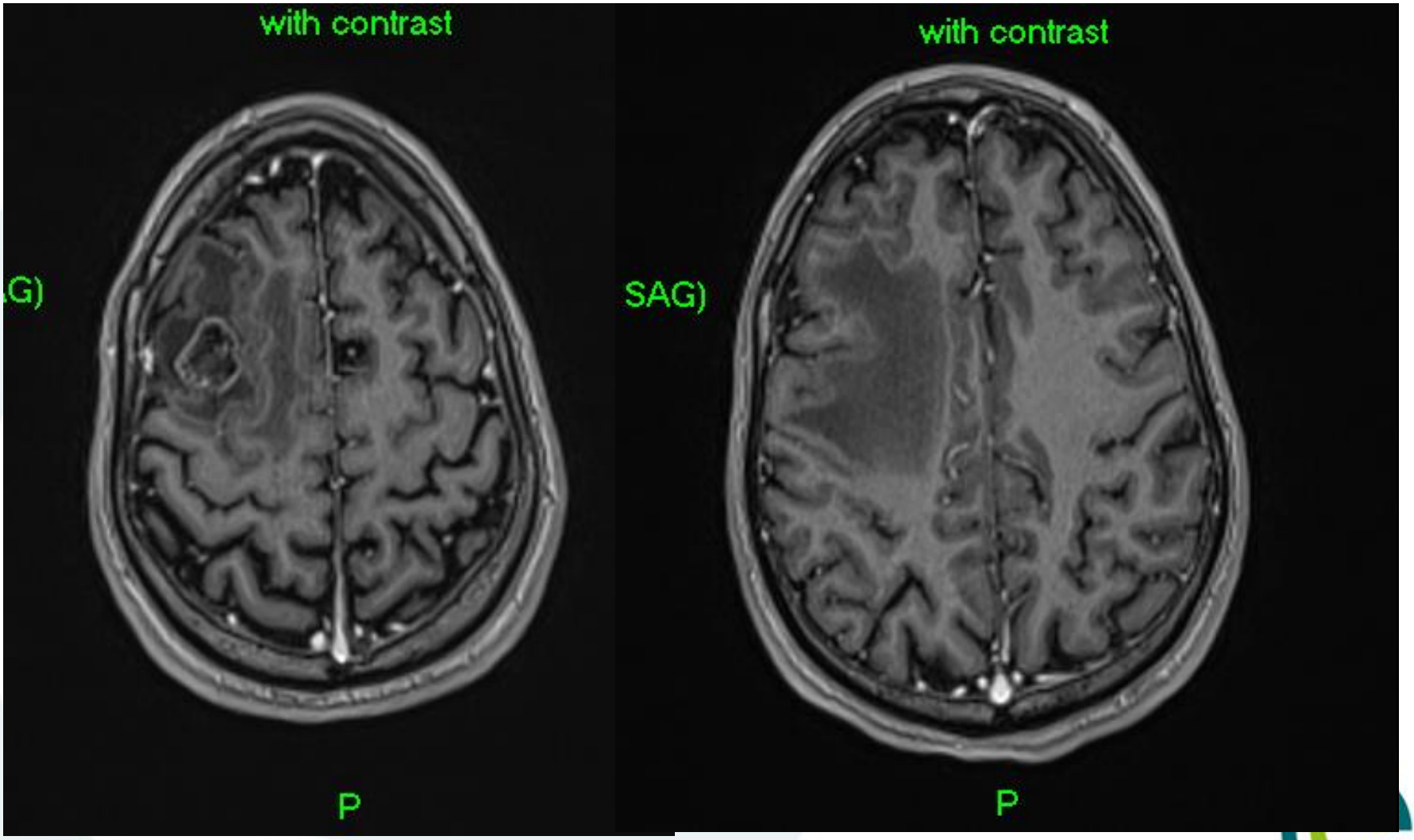

Case 3 A.H.

- Discussed in MDT
  - For resection (Nov 2016) followed by cavity SRT
- Received SRT Dec 2016
- Developed 2 new tiny nodules at the cavity surface Sept 2018
- ?recurrence or post treatment change
- Decided for monitoring
- Currently still no change so assume post RTx changes and has not had further RTx

Case 3 A.H.

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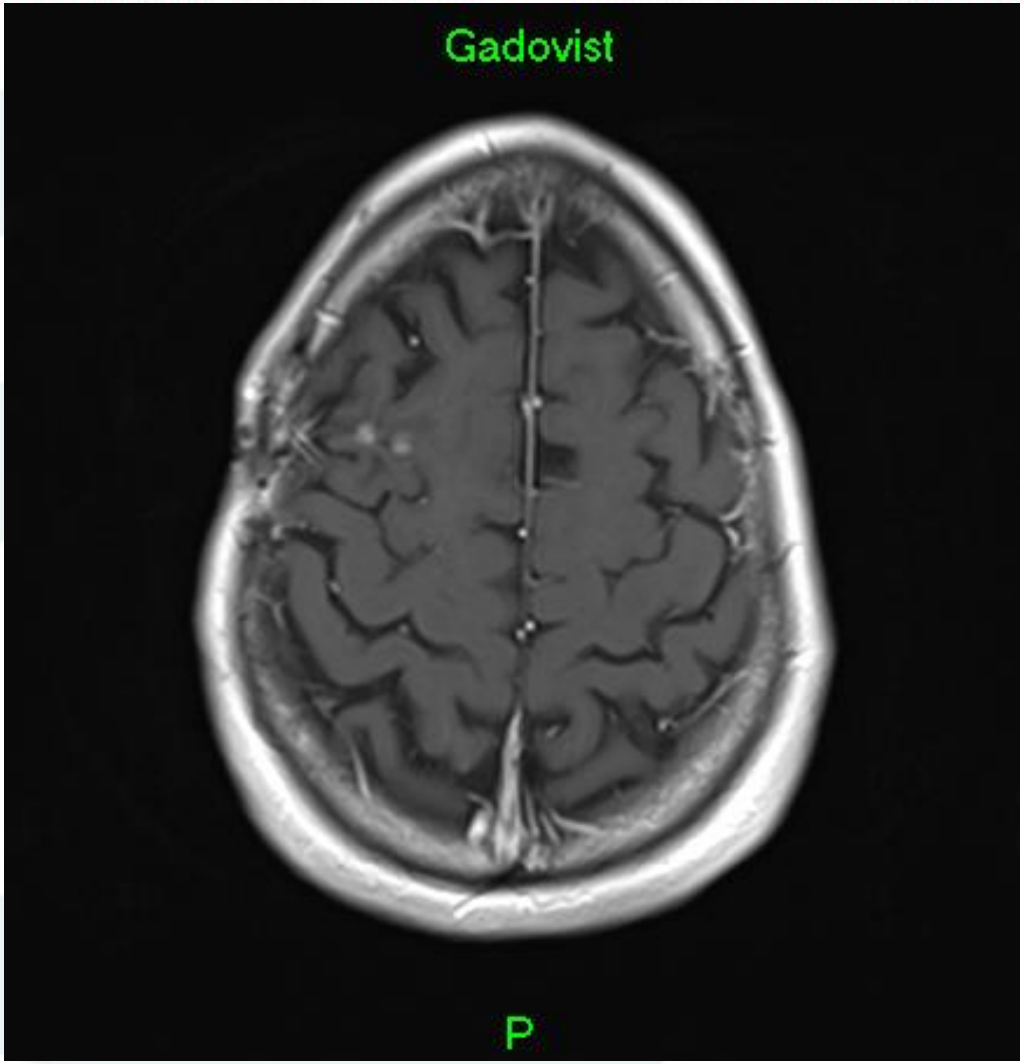
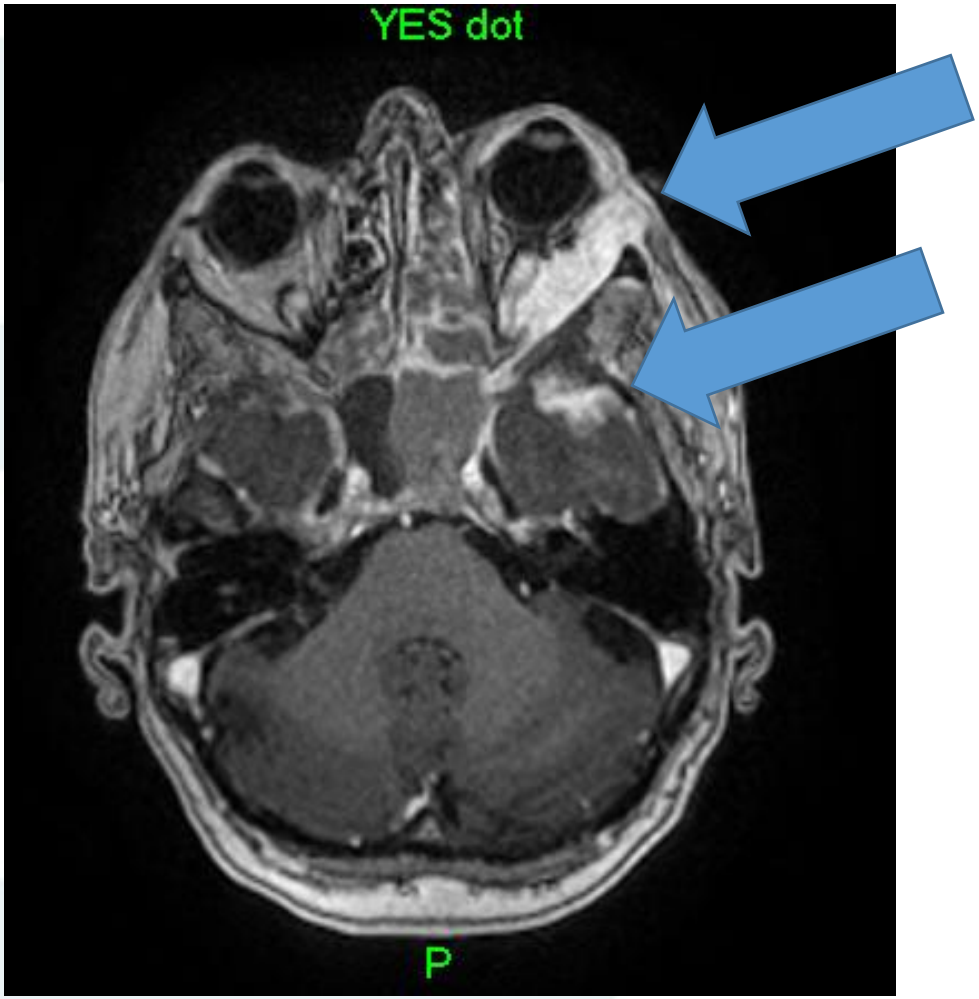


Case 4 G.W.

- 70y female
  - Presented Nov 2015 with extensive bone mets
  - ER +ve HER2 –ve breast cancer
  - Received doxorubicin (briefly) then capecitabine & denosumab
  - Stable disease for 36 months
  - Presented with watery eye, proptosis and double vision
  - MRI showed meningeal disease and left orbital met
  - CT staging – stable extra cranial disease
  - PS 1

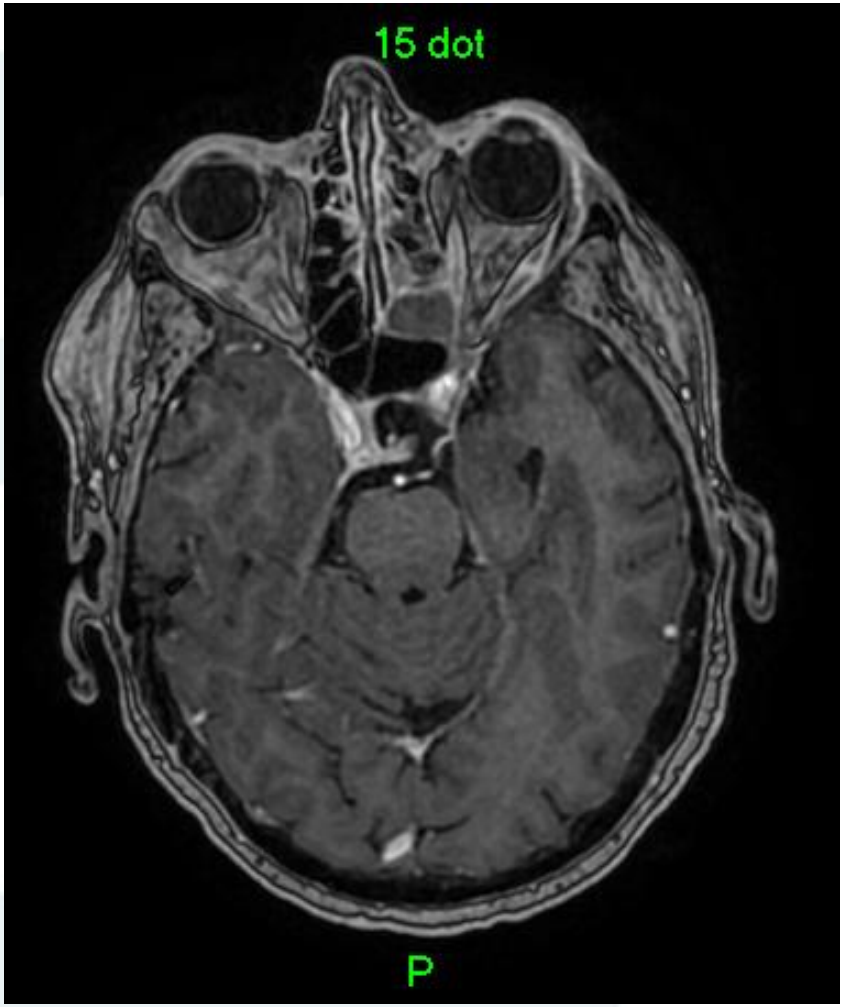
Case 4 G.W.



Case 4 G.W.

- Clearly no surgical option here
- Received WBRT June 2018
- Commenced palbociclib and letrozole
- Remained stable for 17 months
- Last month had extra cranial disease progression and commenced paclitaxel
- Prognosis???

Case 4 G.W.



Case 5 A.C.

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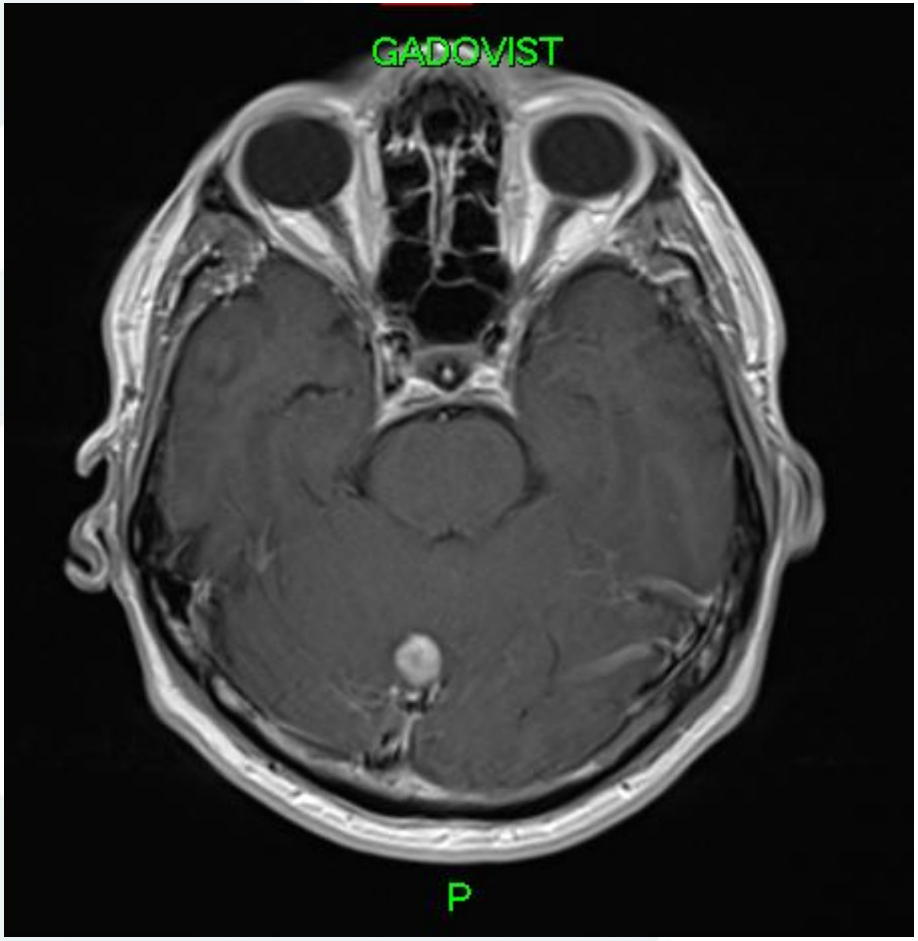
- 49y old male
  - August 2015 – Melanoma left foot, node positive: wide excision, groin dissection and RTx to groin
  - June 2017 – multiple in transit recurrences left leg
  - March 2018 – commenced pembrolizumab
  - May 2019 – disease progression, required full staging for trial entry
  - June 2019 – staging MRI head showed solitary cerebellar metastasis (asymptomatic)

Case 5 A.C.



Case 5 A.C.

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- PS 1
- Not for surgery at MDT
- Received SRS to cerebellar met 25/7/19
- Headaches after
- Commenced trial (Replimune 1 and ipilimumab)
- Rapid deterioration – repeat MRI showed meningeal disease
- Patient died 2/9/19

Case 5 A.C.

- This is a disadvantage of SRS rather than WBRT
  - His meningeal disease would have been there but occult on imaging
  - This is probably happening
- But would it have made any difference?

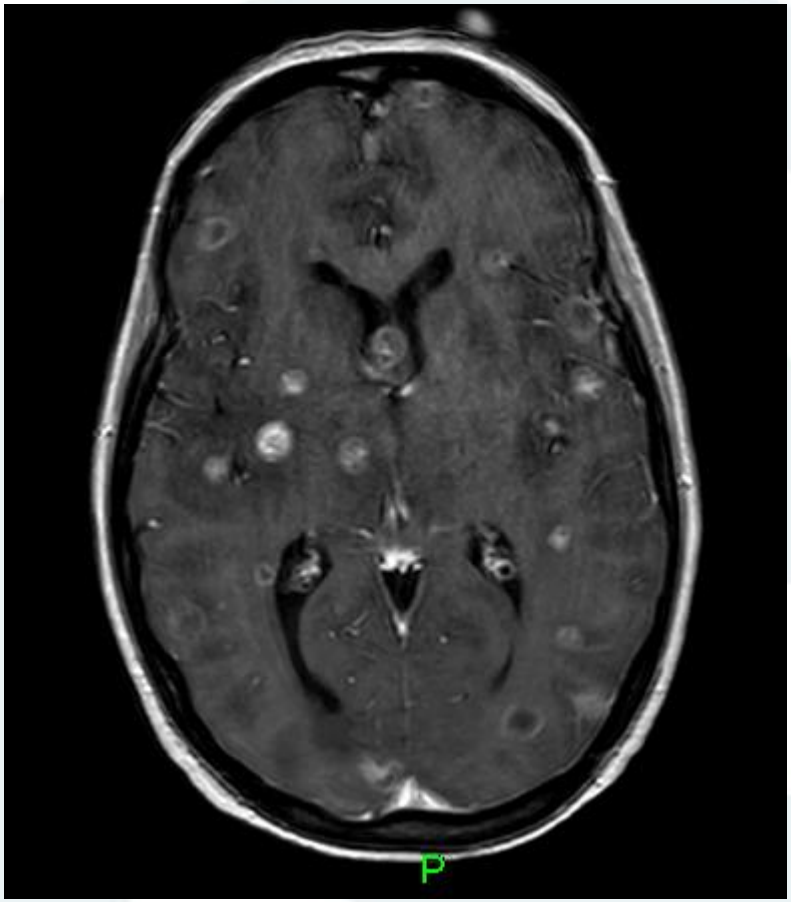
Case 6 S.S.

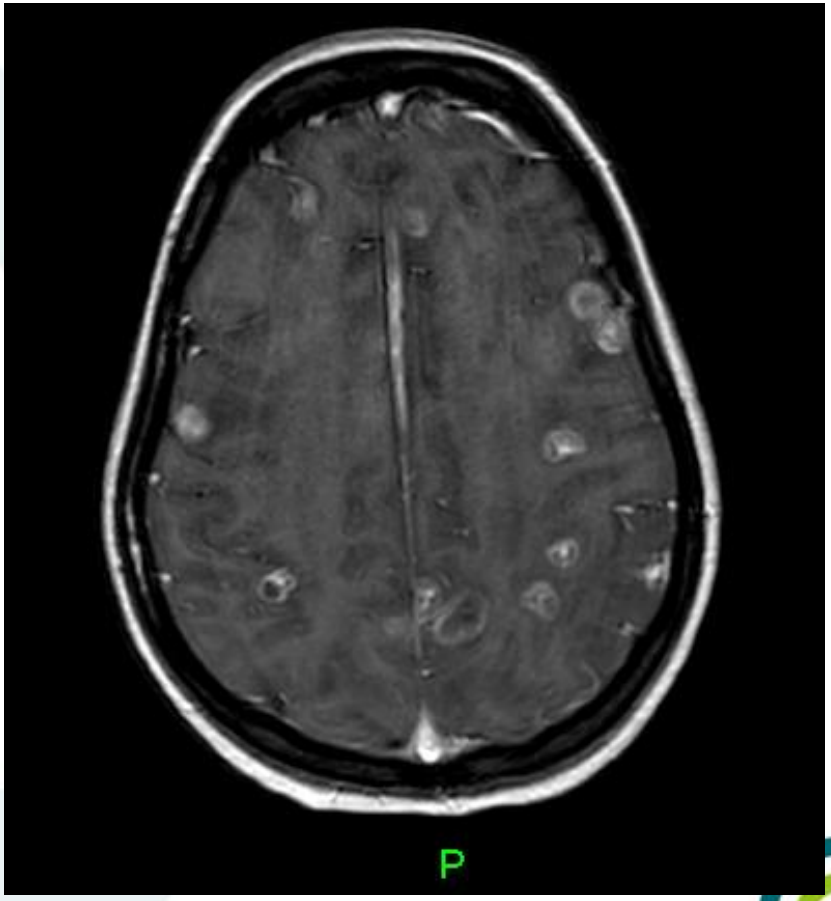
- 48y female
  - May 2012 breast cancer, node positive, ER -ve HER2+ve
  - 2016 bone mets, commenced denosumab and Herceptin x 82 cycles
  - Feb 2019 disease progression, commenced weekly paclitaxel x 6
  - May 2019 disease progression, commenced Kadcyla (TDM-1)

Case 6 S.S.

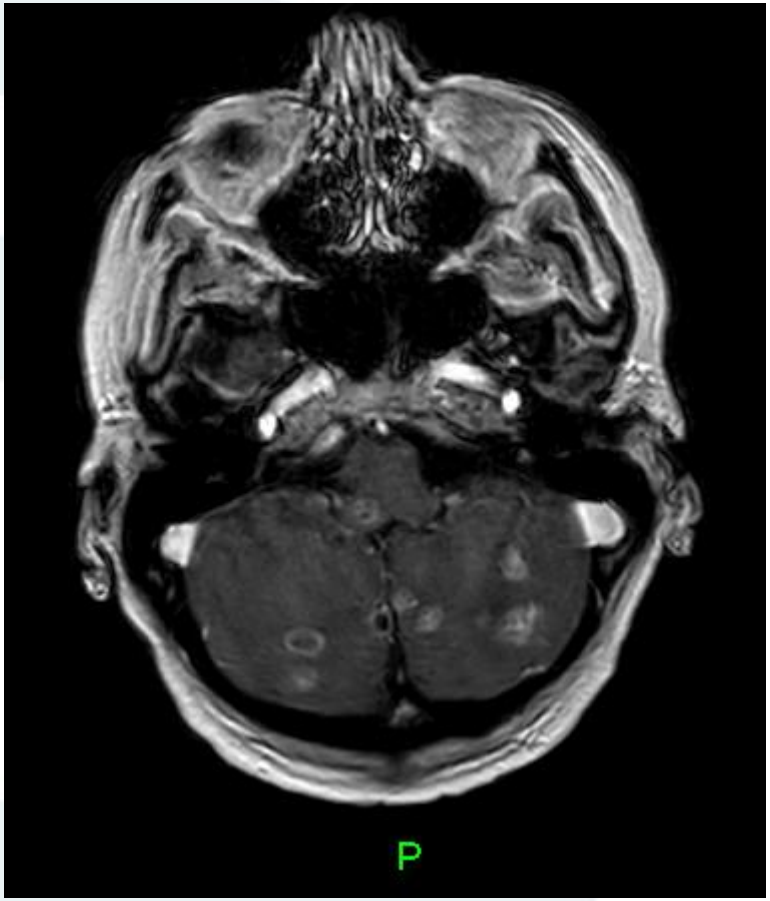
- 3 weeks ago attended A&E with headaches, vomiting and confusion
- CT head showed oedema but no discrete masses
- MRI head shows innumerable metastases

Case 6 S.S.





Case 6 S.S.



Case 6 S.S.

- Commenced dex
- Has seen her clinical oncologist to discuss WBRT pros and cons
- PS 1 – 2 and has decided for WBRT
- The other option is BSC of course

Time for discussion

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- Any questions?

References

- Summary report on the graded prognostic assessment: an accurate and facile diagnosis-specific tool to estimate survival for patients with brain metastases. Sperduto PW, Kased N, Roberge D, Xu Z, Shanley R, Luo X, Sneed PK, Chao ST, Weil RJ, Suh J, Bhatt A, Jensen AW, Brown PD, Shih HA, Kirkpatrick J, Gaspar LE, Fiveash JB, Chiang V, Knisely JP, Sperduto CM, Lin N, Mehta M. J Clin Oncol. 2012 Feb 1;30(4):419-25. doi: 10.1200/JCO.2011.38.0527. Epub 2011 Dec 27.