Low grade astrocytomas:

- 15% of intracranial tumours and 25% of brain gliomas. Median age of patients 35 years.M-55-65%. Mostly sporadic, rarely part of genetic syndromes NF1, TS, Turcot and Li-Fraumeni syndromes. Mostly supratentorial (frontal, temporal and basal ganglia but can occur anywhere).
- The most common presentation is epilepsy (50%).less commonly focal deficit and increased ICP.
- CT scan-hypodense lesion with no enhancement and minimal mass effect can be missed by CT scan. MRI-hyperintense lesion on T2 and FLAIR. PET scan-cold lesion (low metabolism of flourodeoxyglucose). Although the imaging appearance is characteristic, biopsy is needed for definite diagnosis. In one study 45% of no enhancing lesions were AA. 4% of GBM showed no enhancement.
- Histology as above fibrillary, protoplasmic and gemistocytic. **KI-67** index is low in low grade gliomas **2.5-3.5**%. Poor correlation with survival, expression of p53 is poorly correlated with survival or tumour progression, immunostaining for proliferating cell nuclear antigen. (PCNA) >50% is associated with shorter survival.
- Incidence of malignancy: **13-83 %** of recurrent tumours show dedifferentiation to higher grade. This partially due to sampling error and partially due to progression. Carcinogenesis is multistep process that involves multiple genetic alteration(mutation of p53 is found in 1/3 of all gliomas, mutation of another tumour suppressor gene on chromosome 22 , p19 (chromosome 9 and 16) and Rb gene (chromosome 13q) may cause progression to AA and overexpression of EGFR (7p) and PTEN (10Q) gene may cause progression to GBM (Theory)

Discuss controversies in the management of low grade gliomas including timing and extent of surgery and adjuvant therapy: controversial. No class 1-2 evidence**:**

A. Surgery: surgery is necessary to establish the diagnosis (4% of GBM and up to 40% of AA do not enhance), relief of mass effect, control of intractable seizures and possibly decrease in the dedifferentiation into high grade.

Time and extent of surgery: resection of the lesion provides less chance of misdiagnosis (sampling error), provides relief of mass effect, control of intractable seizures and possibly decreases the possibility of dedifferentiation into high grade (Berger showed that 100% resection was associated with no recurrence at 54 month follow up and the recurrence rate was inversely related to the amount of residual tumour). Other studies showed no difference in the progression rate and survival in the group treated immediately and the group treated after demonstration of tumour growth or enhancement.

In summary, complete excision of the lesion, if can be done safely, is recommended for accurate diagnosis and because of the decrease risk of recurrence and improved survival as documented in many published studies

B. Radiotherapy: controversial .No class one evidence in favour of postoperative RT. Retrospective studies showed conflicting results. Radiotherapy may be associated with significant complications. My conclusion is that radiotherapy is indicated if the histology reveals high grade tumour.

Residual low grade tumour should be followed by serial imaging with reoperation if it enlarges. If surgery is risky then RT is an option

C. Chemotherapy: one prospective randomised study showed no difference in survival when chemotherapy was added to radiotherapy.

5 year survival is 50-60% and 10 year survival is 20-40%. Death from local recurrence and dedifferentiation into malignant tumour.

Interpreting the results of the published literature is difficult because of the following reasons:

1. Most published retrospective studies included heterogenous group of patients under the umbrella of low grade gliomas (children with pilocystic astrocytomas, OD etc…)
2. Selection bias: most studies do not state there selection criteria of the type of treatment performed. Younger patients with good functional status are more with accessible tumours are more likely to undergo resection
3. Studies evaluating the extent of resection on the outcome were base on the surgeons assessment of the completeness of resection and not on postoperative volumetric imaging