

Notes by Joan B. Martin MD

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METRONOMIC PHOTODYNAMIC THERAPY: PRINCIPLE TO PRACTICE

Stuart Bisland, University of Toronto

- Novel, alternate strategy aimed at maximizing PDT induced apoptotic cell death in brain tumor
- Debulk tumor with high dose
- Then mPDT may provide better targeting of microfoci distant from the primary lesion
- Are delivering a lower dose: so is oxygen-conserving which determines the inflammatory response and outcome

Research on Gliomas

- 3% of cancer mortality
- 6th most common cause of cancer death over age 20
- Do not metastasize outside CNS
- Surgeon has to take out more than 90% of tumor but highly invasive, difficult to see the margins
- ALA-PDT: have to use low dose or cause necrosis in normal tissue
- Passive diffusion through blood brain barrier (BBB)
- Crosses BBB better in tumor, tumor takes up a little better
- ALA transformed to PpIX
- Nicotinamide enhances results
- Metronomic dosing for PDT entails the concomitant administration of low dose photosensitizing agent and excitation light over prolonged periods of time
- Not getting all the cells with the current TX—can they ever kill enough cells?
- Single treatment after resections doesn't help much
- But can improve outcomes with ALA mediated fluorescent guided resection: 3 fold improvement in survival
- Future of PDT
 - Surgical resection of bulk tumor
 - Unresectable macroscopic tumor: acute high dose PDT plus mPDT
 - Technology not there yet for delivering the light
- Conclusions
 - ALA is good candidate of mPDT in brain
 - MPDT favors apoptosis in the brains
 - Adjuvants may help
 - Metronomic light delivery is a challenge
 - Acute PDT can debulk the tumor
 - MPDT addresses the true clinical dilemma of oxygen depletion
 - Have to debulk >90% to see any improvement in survival
 - Improved dosimetry is needed

Questions: 5ALA used for tiny skin tumors, Bowen's ds—need to find balance between amount of drug and amount of light
Treatment enhances angiogenesis, activates endothelial growth factor
Biostimulation + PDT, protoporphyrin 9 stimulated within the mitochondria, has not yet been tried