Developments in Neurosurgery for Brain Tumours:
Subspecialisation & Patient Experience

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Summary

- Why are brain tumours important? “Size of the problem”
- Recent advances in surgical management
- Impact of these on patients: Survival and quality of life

Primary Brain Tumours

- Less than 2% of all tumours
- 3rd leading cause of cancer-related death amongst population between 15-54 years of age
- Gliomas are the commonest of primary brain tumours
- High grade gliomas the most aggressive and difficult to treat

As an intervention, surgery has the most significant impact on the survival and quality of life of patients with brain tumours.

The Past

Prognosis & management of glioblastomas remain unchanged in decades with a median survival of 6-9 months

Key Recent Advances

- Image guidance
- Functional imaging
- Intra-operative mapping
- Awake surgery
- Fluorescent resection
- Intra-operative chemotherapy
- **Change in management philosophy**

Modern Surgical Philosophy:

Radical Resection

Volumetric extent of resection studies in High-Grade Glioma

Study	Tumor grade(s)	Patients	Extent of resection (*n*)	Overall survival		
				Mean survival (months)	Univariate analysis *P* value	Multivariate analysis *P* value
Keles *et al.* [12]	IV	107	<25% (25)	8.0	NA	<0.0005
			25–49% (21)	14.2		
			50–74% (18)	15.7		
			75–99% (20)	22.1		
			100% (23)	23.3		
Pope *et al.* [21]	IV	110	<20%	27.4	NS	NS
			20–89%	11.1		
			90–99%	17.1		
			100%	22.1		
Lacroix *et al.* [15]	IV	416	<98%	8.8	<0.0001	<0.0001
			≥98%	13.0		
Keles *et al.* [13]	III	102	0–100%	41.0	NS	NS
Sanai *et al.* 2011 [32▪]	IV	500	>77%	12.5	<0.0001	0.004
			>79%	12.8		
			>89%	13.8		
			100%	16		

Intra-operative Imaging

Navigation

iMRI

iUSS

Functional Imaging: fMRI

Surgical Neurology 2005;64:20: Retrospective study, good accuracy

Motor **Language**

Transcranial Magnetic Stimulation

Intra-Operative Cortical and subcortical mapping

- Stimulation done either awake or asleep for motor function
- Always done awake for Speech
- Stimulation either
    - Inhibitory – speech
    - Stimulatory – Motor Movement
- Continuous EcoG and SSEPS, MEPS running in background if patient asleep
- Continuous Movement and Speech if patient awake
- Can stimulate both Cortex and Sub- Cortical White Matter Tracts

Fluorescent guided resection

Gliolan: Intra operative 5 ALA

- 5ALA is differentially taken up by glioma cells and is converted into protoporphyrin
- The chemical fluoresces under blue light giving the glioma cells a red colour, thus distinguishing them from normal brain
- Study in high grade glioma showing gliolan increasing tumour resection and progression free survival
- Side effect: skin photosensitivity for 24 hours

Intra operative chemotherapy: Gliadel

Means of killing residual tumour cells in the surgical cavity

Gliadel: Intra operative chemotherapy

- NICE 2007: Carmustine implants
- Study in high grade glioma showing median survival of 13.8 months with carmustine versus 11.6 months without

Recommendations:

- High grade gliomas (first diagnosis); need for intra-operative histopathology
- Must remove at least 90% of tumour
- Use of neuronavigation to achieve maximal resection
- Must have complete dural closure
- There must be no opening into the ventricles
- Maximum 8 wafers (about 60 mg)

GALA-5

An Evaluation of the Tolerability and Feasibility of combining 5-Amino-Levulinic Acid (5-ALA) with Carmustine Wafers (Gliadel) in the Surgical Management of Primary Glioblastoma.

Single arm feasibility trial involving 60 patients to establish the safety, tolerability and feasibility of combining fluorescence-guided surgical brain tumour resection with intra-operative chemotherapy in patients with primary glioblastoma prior to standard treatment with radiotherapy and temozolomide.

Current Developments

- ✓ Immunotherapy: DCVax, *towards individualised therapy*
- ✓ Molecular stratification of tumours, *beyond IDH, 1p/19q, MGMT, ATRX etc*
- ✓ Nanotechnology, *towards gene detection and repair*

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REVIEW ARTICLE

Active dendritic cell immunotherapy for glioblastoma: Current status and challenges

Stavros Polyzoidis[1], Juel Tuazon[2], Lucy Brazil[3], Ronald Beaney[3], Safa Taha Al-Sarraj[4], Lawrence Doey[4], Jamie Logan[5], Victoria Hurwitz[5], Jozef Jarosz[6], Ranjeev Bhangoo[1], Richard Gullan[1], Aleksandar Mijovic[7], Mark Richardson[8], Farzin Farzaneh[9] & Keyoumars Ashkan[1]

- Median overall survival ranged between 16.0-38.4 months for ND-GBM and between 9.6-35.9 months for Rec-GBM.
- Vaccine-related side effects were in general mild
- DC immunotherapy has the potential to increase the overall survival in patients with HGG, with an acceptable side effect profile.

Genetics

ORIGINAL ARTICLE

Glioma Groups Based on 1p/19q, *IDH*, and *TERT* Promoter Mutations in Tumors

- Classified into five principal groups on the basis of three tumor markers.
- The groups had different ages at onset, and survival.

- Associations with germline variants, which implies that they are characterized by distinct mechanisms of pathogenesis.

Genomics England

Genomics England announced by NHS England during NHS 65th Anniversary Celebrations, July 2013

£300 m funding

"It is crucial that we continue to push the boundaries and this new plan will mean we are the first country in the world to use DNA codes in the mainstream of the health service"

Whole genome sequencing of 100,000 genomes: Rare disease and Cancers

Modern Management of High Grade Gliomas

- Prognosis still poor

BUT

- Advanced surgical techniques combined with multi-modal therapy has now increased median survival > 18 months compared to 6-9 months only 10 years ago (survival)

- Such advances are also increasing the safety of surgery helping to preserve and improve quality of life of patients

Quality of life is harder to measure!

Support Care Cancer (2014) 22:2965–2972
DOI 10.1007/s00520-014-2291-3

ORIGINAL ARTICLE

Neurobehavioural changes in patients following brain tumour: patients and relatives perspective

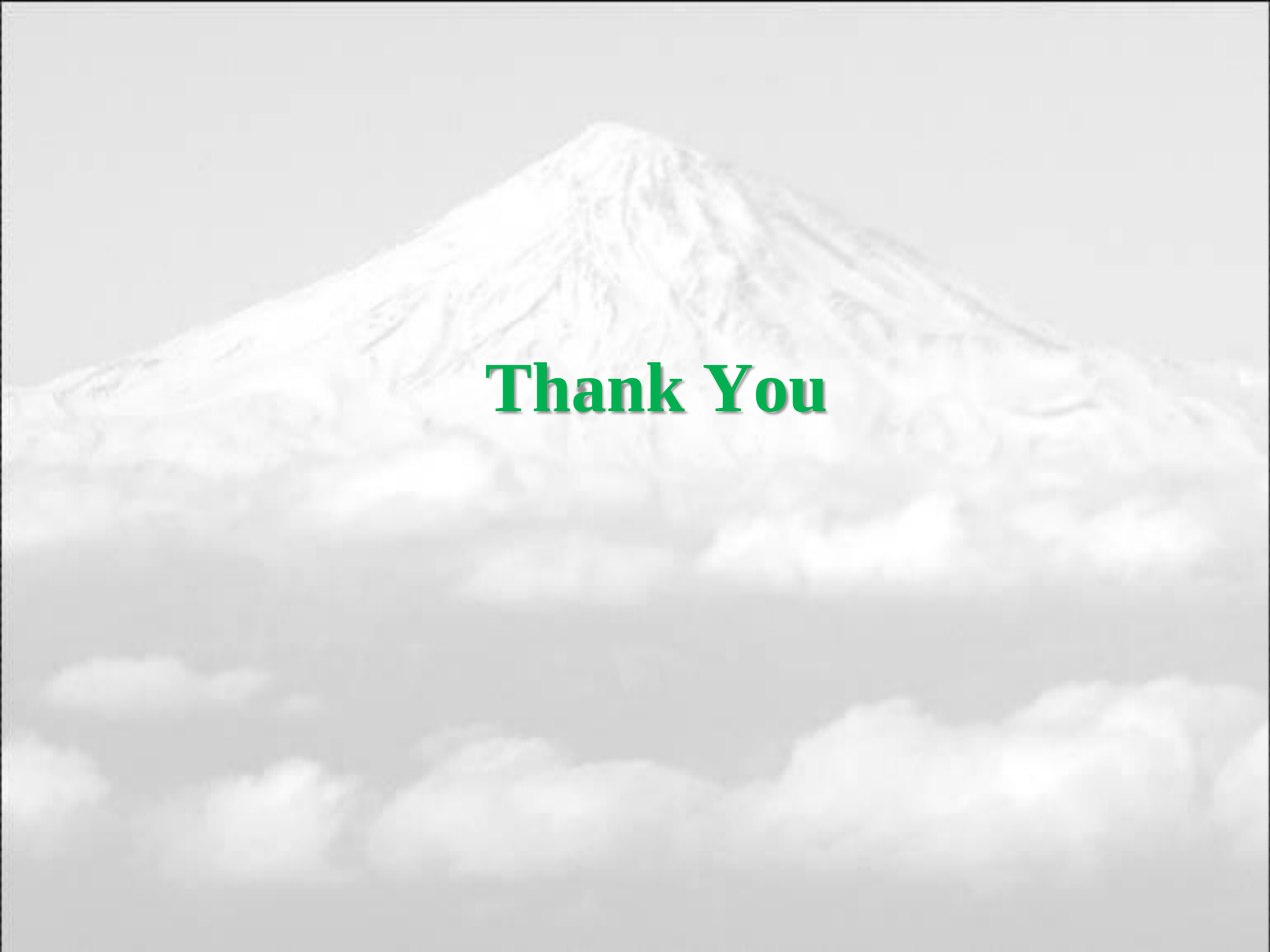
N. Gregg · A. Arber · K. Ashkan · L. Brazil · R. Bhangoo · R. Beaney · R. Gullan · V. Hurwitz · A. Costello · L Yágüez

Conclusion: Support and management of behavioural and personality change for patients with brain tumours and their
relatives, regardless of tumour location, would be most appropriate.

Concluding Remarks

- Surgical technology has developed rapidly in recent years
- BUT there is still much room for progress!
- Also surgery is only [illegible] solution!
- [illegible] continue to work together to address the needs [illegible] spectrum of our patients
- Improving survival is a challenge but optimizing the quality is perhaps the harder problem

As CNSs and AHPs you are the ones with the hardest task!


Thank You