

# Patient and Caregiver Perspective: Diagnosed with Brain Metastases

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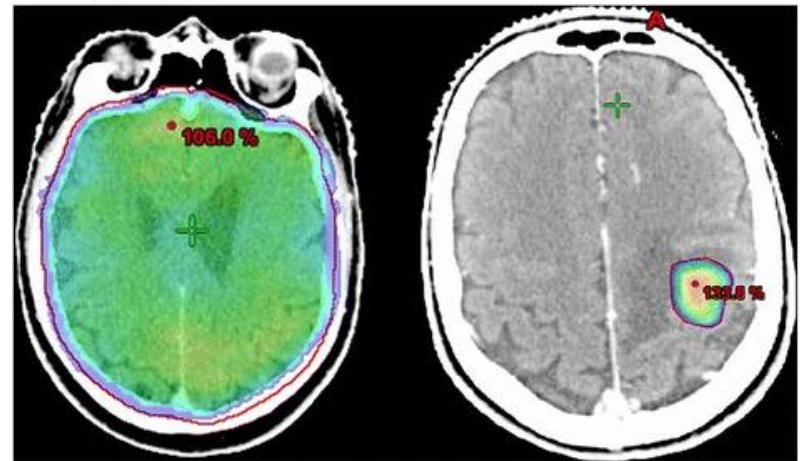
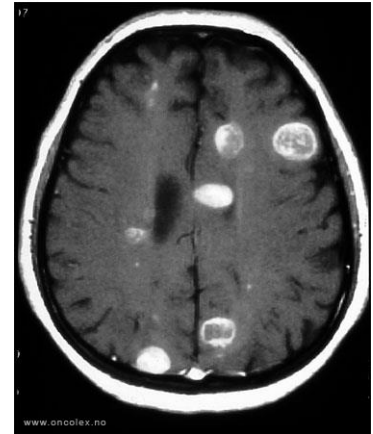
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7th of October 2017

# Outline

- Diagnosed with brain metastases
  - The patient's perspective
  - The caregiver's perspective
  - The treatment of brain metastases
- The patient's perspective in studies
  - Why?
  - How?
  - Challenges
  - Example: The QUARTZ trial
- Future perspectives

# Diagnosed with brain metastases

- Primary cancer diagnosis
- Brain metastases
  - Treatment toxicities and side effects
    - Surgery
    - Radiation therapy
    - Systemic therapies
  - Cognitive decline



[www.oncolex.org](http://www.oncolex.org); Zindler *et al.*, BMC Cancer, 2017

# Diagnosed with brain metastases: the patient's perspective

- Symptoms
  - Altered mental status, imbalance, and visual impairments. Headaches, fatigue, and focal weakness [1]
- Informational needs
  - Prognosis, managing symptoms, and available treatment options and associated side effects [2]
- Compared to primary brain cancer
  - Emotional strain and anxiety more prevalent [3]

[1] Wong *et al.*, Support Care Cancer, 2016

[2] Maqbool *et al.*, J Canc Educ, 2016

[3] Ostgathe *et al.*, Support Care Cancer, 2010

# Diagnosed with brain metastases: the caregiver's perspective

- “An overwhelming and unpredictable role”
  - Due to the patient's cognitive and functional decline [1]
- Psychiatric disorders
  - Screened: 345 caregivers of advanced cancer patients
  - 52% had one or more suspected psychiatric disorders [2]

[1] Saria *et al.*, Nurs Clin North Am, 2017

[2] Rumpold *et al.*, Support Care Cancer, 2016

# Brain metastases: Randomized clinical trials

- Primary endpoint overall survival:
  - Brown *et al.*, Lancet Oncol, 2017
    - “Postoperative stereotactic radiosurgery compared with whole brain radiotherapy for resected metastatic brain disease”
  - Kocher *et al.*, JCO, 2011
    - “Adjuvant Whole-Brain Radiotherapy Versus Observation After Radiosurgery or Surgical Resection”
  - Aoyama *et al.*, JAMA, 2006
    - “Stereotactic Radiosurgery Plus Whole-Brain Radiation Therapy vs Stereotactic Radiosurgery Alone”

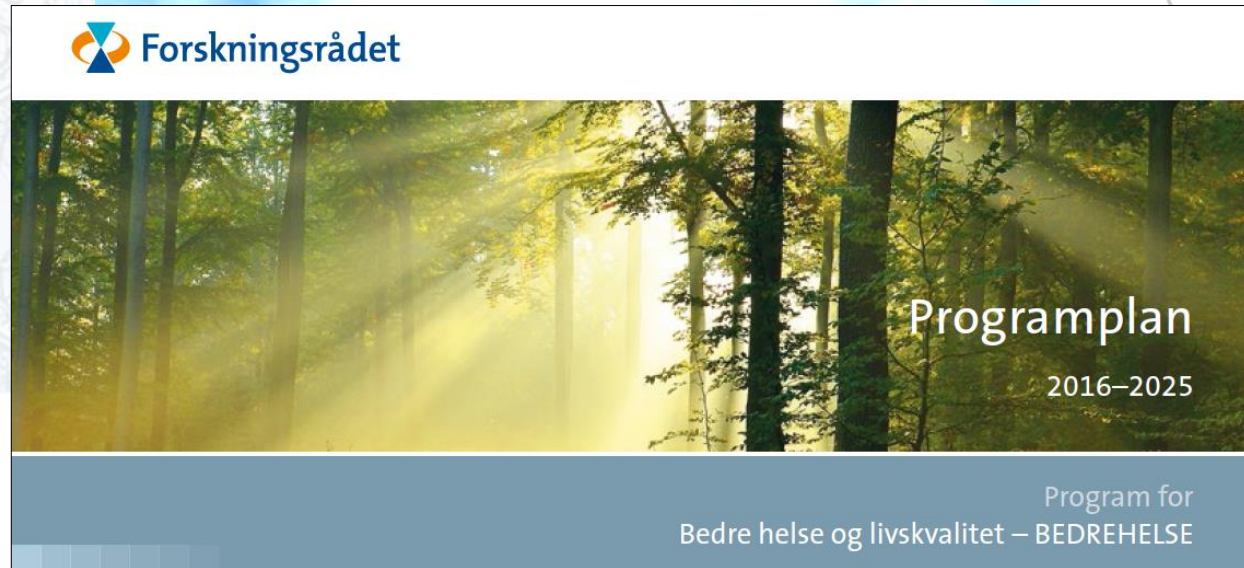
# Brain metastases: Randomized clinical trials

- Primary endpoint overall survival
  - Brown *et al.*, Lancet Oncol, 2017
    - ...no difference in overall survival
  - Kocher *et al.*, JCO, 2011
    - ...fails to improve overall survival
  - Aoyama *et al.*, JAMA, 2006
    - ...did not improve survival



# The patient's perspective should be included in studies

- Quality of life is the main goal of palliative care
- Independent predictor of survival [1]
- The law
- Influence
- Money



[1] Gotay *et al.*, JCO, 2008




# How can the patient's perspective be assessed?

- Patient – health care provider
- Questionnaires
- In-depth interviews
  - Open
  - Semi-structured
  - Structured
- Observation
  - Proxy-ratings: caregiver or health care provider

# Patient-reported outcomes

- Questionnaires
  - EORTC QLQ-BN20

ENGLISH



**EORTC QLQ - BN20**

Patients sometimes report that they have the following symptoms. Please indicate the extent to which you have experienced these symptoms or problems during the past week.

---

**During the past week:**

	Not at All	A Little	Quite a Bit	Very Much
31. Did you feel uncertain about the future?	1	2	3	4
32. Did you feel you had setbacks in your condition?	1	2	3	4
33. Were you concerned about disruption of family life?	1	2	3	4
34. Did you have headaches?	1	2	3	4
35. Did your outlook on the future worsen?	1	2	3	4
36. Did you have double vision?	1	2	3	4
37. Was your vision blurred?	1	2	3	4
38. Did you have difficulty reading because of your vision?	1	2	3	4
39. Did you have seizures?	1	2	3	4
40. Did you have weakness on one side of your body?	1	2	3	4
41. Did you have trouble finding the right words to express yourself?	1	2	3	4
42. Did you have difficulty speaking?	1	2	3	4
43. Did you have trouble communicating your thoughts?	1	2	3	4
44. Did you feel drowsy during the daytime?	1	2	3	4
45. Did you have trouble with your coordination?	1	2	3	4
46. Did hair loss bother you?	1	2	3	4
47. Did itching of your skin bother you?	1	2	3	4
48. Did you have weakness of both legs?	1	2	3	4
49. Did you feel unsteady on your feet?	1	2	3	4
50. Did you have trouble controlling your bladder?	1	2	3	4

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# Patient-reported outcomes

- Questionnaires
  - EORTC QLQ-BN20
  - FACT-Brain

ENGLISH

**FACT-BR (Version 4)**

Below is a list of statements that other people with your illness have said are important. By circling one (1) number per line, please indicate how true each statement has been for you during the past 7 days.

		Not at all	A little bit	Some-what	Quite a bit	Very much
<b><u>PHYSICAL WELL-BEING</u></b>						
OP1	I have a lack of energy.....	0	1	2	3	4
OP2	I have nausea.....	0	1	2	3	4
OP3	Because of my physical condition, I have trouble meeting the needs of my family.....	0	1	2	3	4
OP4	I have pain.....	0	1	2	3	4
OP5	I am bothered by side effects of treatment.....	0	1	2	3	4
OP6	I feel ill.....	0	1	2	3	4
OP7	I am forced to spend time in bed.....	0	1	2	3	4
<b><u>SOCIAL/FAMILY WELL-BEING</u></b>						
OS1	I feel close to my friends.....	0	1	2	3	4
OS2	I get emotional support from my family.....	0	1	2	3	4
OS3	I get support from my friends.....	0	1	2	3	4
OS4	My family has accepted my illness.....	0	1	2	3	4
OS5	I am satisfied with family communication about my illness.....	0	1	2	3	4
OS6	I feel close to my partner (or the person who is my main support).....	0	1	2	3	4
OS	<i>Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please check this box <input type="checkbox"/> and go to the next section.</i>					
OS7	I am satisfied with my sex life.....	0	1	2	3	4

# Patient-reported outcomes

- Questionnaires
  - EORTC QLQ-BN20
  - FACT-Br
  - EQ-5D

ENGLISH

**Figure 1: EQ-5D-5L (UK English sample version)**

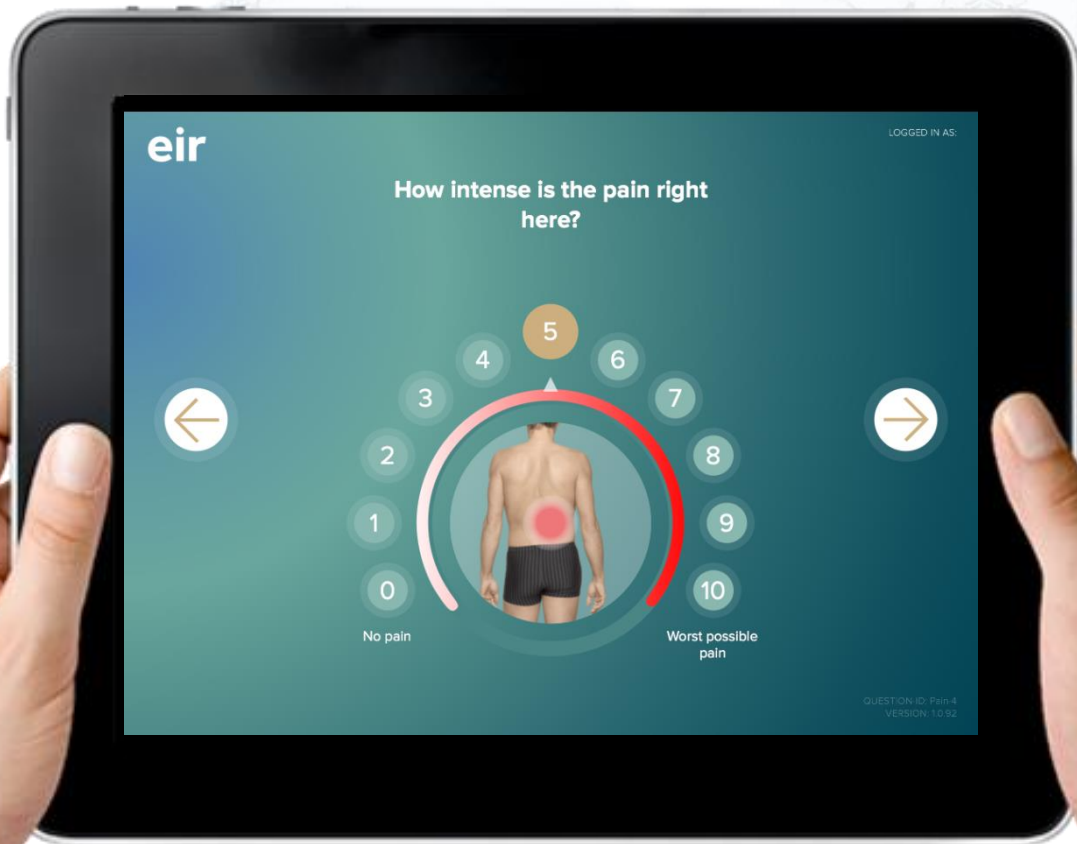
Under each heading, please tick the ONE box that best describes your health TODAY

Below is a list of statements. Please circle one box for each statement during the past 7 days.

<p>op1 I have no problems in walking about</p> <p>op2 I have slight problems in walking about</p> <p>op3 I have moderate problems in walking about</p> <p>op4 I have severe problems in walking about</p> <p>op5 I am unable to walk about</p>	<p><b>MOBILITY</b></p> <p>I have no problems in walking about <input type="checkbox"/></p> <p>I have slight problems in walking about <input type="checkbox"/></p> <p>I have moderate problems in walking about <input type="checkbox"/></p> <p>I have severe problems in walking about <input type="checkbox"/></p> <p>I am unable to walk about <input type="checkbox"/></p>
<p>op6 I have no problems washing or dressing myself</p> <p>op7 I have slight problems washing or dressing myself</p> <p>op8 I have moderate problems washing or dressing myself</p> <p>op9 I have severe problems washing or dressing myself</p> <p>op10 I am unable to wash or dress myself</p>	<p><b>SELF-CARE</b></p> <p>I have no problems washing or dressing myself <input type="checkbox"/></p> <p>I have slight problems washing or dressing myself <input type="checkbox"/></p> <p>I have moderate problems washing or dressing myself <input type="checkbox"/></p> <p>I have severe problems washing or dressing myself <input type="checkbox"/></p> <p>I am unable to wash or dress myself <input type="checkbox"/></p>
<p>op11 I have no problems doing my usual activities</p> <p>op12 I have slight problems doing my usual activities</p> <p>op13 I have moderate problems doing my usual activities</p> <p>op14 I have severe problems doing my usual activities</p> <p>op15 I am unable to do my usual activities</p>	<p><b>USUAL ACTIVITIES</b> (e.g. work, study, housework, family or leisure activities)</p> <p>I have no problems doing my usual activities <input type="checkbox"/></p> <p>I have slight problems doing my usual activities <input type="checkbox"/></p> <p>I have moderate problems doing my usual activities <input type="checkbox"/></p> <p>I have severe problems doing my usual activities <input type="checkbox"/></p> <p>I am unable to do my usual activities <input type="checkbox"/></p>
<p>op16 I have no pain or discomfort</p> <p>op17 I have slight pain or discomfort</p> <p>op18 I have moderate pain or discomfort</p> <p>op19 I have severe pain or discomfort</p> <p>op20 I have extreme pain or discomfort</p>	<p><b>PAIN / DISCOMFORT</b></p> <p>I have no pain or discomfort <input type="checkbox"/></p> <p>I have slight pain or discomfort <input type="checkbox"/></p> <p>I have moderate pain or discomfort <input type="checkbox"/></p> <p>I have severe pain or discomfort <input type="checkbox"/></p> <p>I have extreme pain or discomfort <input type="checkbox"/></p>
<p>op21 I am not anxious or depressed</p> <p>op22 I am slightly anxious or depressed</p> <p>op23 I am moderately anxious or depressed</p> <p>op24 I am severely anxious or depressed</p> <p>op25 I am extremely anxious or depressed</p>	<p><b>ANXIETY / DEPRESSION</b></p> <p>I am not anxious or depressed <input type="checkbox"/></p> <p>I am slightly anxious or depressed <input type="checkbox"/></p> <p>I am moderately anxious or depressed <input type="checkbox"/></p> <p>I am severely anxious or depressed <input type="checkbox"/></p> <p>I am extremely anxious or depressed <input type="checkbox"/></p>

# Patient-reported outcomes

- Electronic



# Patient-reported outcomes

- Challenges
  - Methodological limitations
    - Selection bias
    - Missing data
    - Timing of assessment
  - Clinically relevant change?
  - Patients with cognitive decline



# Patient-reported outcomes as endpoint: the QUARTZ trial

Dexamethasone and supportive care with or without whole brain radiotherapy in treating patients with non-small cell lung cancer with brain metastases unsuitable for resection or stereotactic radiotherapy (QUARTZ): results from a phase 3, non-inferiority, randomised trial

Paula Mulvenna, Matthew Nankivell, Rachael Barton, Corinne Fäivre-Finn, Paula Wilson, Elaine McColl, Barbara Moore, Iona Brisbane, David Ardon, Tanya Holt, Sally Morgan, Caroline Lee, Kathryn Waite, Neil Bayman, Cheryl Pugh, Benjamin Sydes, Richard Stephens, Mahesh K Parmar, Ruth E Langley

## Summary

Background Whole brain radiotherapy (WBRT) and dexamethasone are widely used to treat brain metastases from

**the absence of a difference in survival and quality of life**

**Methods** The Quality of Life after Treatment for Brain Metastases (QUARTZ) study is a non-inferiority, phase 3 randomised trial done at 69 UK and three Australian centres. NSCLC patients with brain metastases unsuitable for surgical resection or stereotactic radiotherapy were randomly assigned (1:1) to optimal supportive care (OSC) including dexamethasone plus WBRT (20 Gy in five daily fractions) or OSC alone (including dexamethasone). The dose of dexamethasone was determined by the patients' symptoms and titrated downwards if symptoms improved. Allocation to treatment group was done by a phone call from the hospital to the Medical Research Council Clinical Trials Unit at University College London using a minimisation programme with a random element and stratification by centre, Karnofsky Performance Status (KPS), gender, status of brain metastases, and the status of primary lung cancer. The primary outcome measure was quality-adjusted life-years (QALYs). QALYs were generated from overall survival and patients' weekly completion of the EQ-5D questionnaire. Treatment with OSC alone was considered non-inferior if it was no more than 7 QALY days worse than treatment with WBRT plus OSC, which required 534 patients (80% power, 5% [one-sided] significance level). Analysis was done by intention to treat for all randomly assigned patients. The trial is registered with ISRCTN, number ISRCTN3826061.

**Findings** Between March 2, 2007, and Aug 29, 2014, 538 patients were recruited from 69 UK and three Australian centres, and were randomly assigned to receive either OSC plus WBRT (269) or OSC alone (269). Baseline characteristics were balanced between groups, and the median age of participants was 66 years (range 38–85). Significantly more episodes of drowsiness, hair loss, nausea, and dry or itchy scalp were reported while patients were receiving WBRT, although there was no evidence of a difference in the rate of serious adverse events between the two groups. There was no evidence of a difference in overall survival (hazard ratio 1.06, 95% CI 0.90–1.26), overall quality of life, or dexamethasone use between the two groups. The difference between the mean QALYs was 4.7 days (46.4 QALY days for the OSC plus WBRT group vs 41.7 QALY days for the OSC group), with two-sided 90% CI of -12.7 to 3.3.

**Interpretation** Although the primary outcome measure result includes the prespecified non-inferiority margin, the combination of the small difference in QALYs and the absence of a difference in survival and quality of life between the two groups suggests that WBRT provides little additional clinically significant benefit for this patient group.

Mulvenna *et al.*, Lancet, 2016

# Patient-reported outcomes as endpoint: the QUARTZ trial

Dexamethasone and supportive care with or without whole brain radiotherapy in treating patients with non-small cell lung cancer with brain metastases unsuitable for resection or stereotactic radiotherapy (QUARTZ): results from a phase 3, non-inferiority, randomised trial

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### Summary

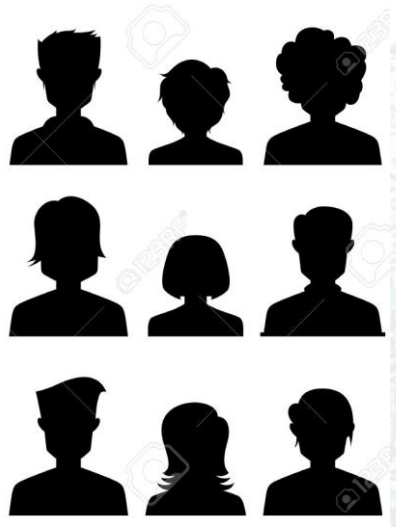
**Background** Whole brain radiotherapy (WBRT) and dexamethasone are widely used to treat brain metastases from non-small cell lung cancer (NSCLC), although there have been no randomised clinical trials showing that WBRT improves either quality of life or overall survival. Even after treatment with WBRT, the prognosis of this patient group is poor. We aimed to establish whether WBRT could be omitted without a significant effect on survival or quality of life.

**Methods** The Quality of Life after Treatment for Brain Metastases (QUARTZ) study is a non-inferiority, phase 3 randomised trial done at 69 UK and three Australian centres. NSCLC patients with brain metastases unsuitable for surgical resection or stereotactic radiotherapy were randomly assigned (1:1) to optimal supportive care (OSC) including dexamethasone plus WBRT (20 Gy in five daily fractions) or OSC alone (including dexamethasone). The dose of dexamethasone was determined by the patients' symptoms and titrated downwards if symptoms improved. Allocation to treatment group was done by a phone call from the hospital to the Medical Research Council Clinical Trials Unit at University College London using a minimisation programme with a random element and stratification by centre, Karnofsky Performance Status (KPS), gender, status of brain metastases, and the status of primary lung cancer. The primary outcome measure was quality-adjusted life-years (QALYs). QALYs were generated from overall survival and patients' weekly completion of the EQ-5D questionnaire. Treatment with OSC alone was considered non-inferior if it was no more than 7 QALY days worse than treatment with WBRT plus OSC, which required 534 patients (80% power, 5% [one-sided] significance level). Analysis was done by intention to treat for all randomly assigned patients. The trial is registered with ISRCTN, number ISRCTN3826061.

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Mulvenna *et al.*, Lancet, 2016



Dorman *et al.*,  
Palliat Med, 2009

# Patient quotes from Dorman *et al.*:

- On quality of life
  - Participant 2: “[Quality] is more important than the time, much more important.”
- On prolonging survival
  - What are you hoping to gain from the radiotherapy?
    - Participant 8: “Well obviously live longer if I could.”
  - What is more important to you, quality of life or the length of life?
    - Participant 9: “The length of life obviously”

Dorman *et al.*, Palliat Med, 2009

# Future perspectives

- Patient-reported outcomes
  - Standardization of study design
    - The Response Assessment in Neuro-Oncology (RANO) group [1]

[1] Lin *et al.*, Lancet Oncol, 2013

# Future perspectives

- Patients with brain metastases
  - Registry study
  - Qualitative study
    - Patients and their caregivers
    - Writing study protocol: Interviews
    - Study design under consideration, prospective follow-up



Happiness is the meaning and the purpose of life, the whole aim and end of human existence.

~ Aristotle

AZ QUOTES