

The background of the slide features a repeating, light-colored floral and damask pattern on a slightly darker background. The pattern consists of stylized leaves, scrolls, and floral motifs arranged in a regular grid.

**EVIDENCE AND QUALITY OF LIFE:
THE WAY FORWARD**

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Intensity-Modulated Radiation Therapy, Proton Therapy, or Conformal Radiation Therapy and Morbidity and Disease Control in Localized Prostate Cancer

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Context There has been rapid adoption of newer radiation treatments such as intensity-

BACKGROUND.....

Photons: good dose distributions, image guidance, accurate machines, in-room imaging facilities for real time imaging and tracking

Impressions about protons: Bragg peak, superior dose distributions...but a superior outcome???

Dosimetric superiority alone does not ensure clinically superior outcomes

WHY WE NEED EVIDENCE?

Its all about money!

If protons were costing the same or less than IMRT

Dosimetric superiority and planning studies would have sufficed

But.....it costs more, and does not seem to change the outcomes *universally*

So, why should patients/governments/insurance pay more?

BACKGROUND CONTD...

Do we need evidence?

YES

Are randomised controlled trials the only acceptable argument for proving a technology?

Maybe not

WHAT IS NEEDED TO BE DONE

Strong phase II trials

Prove clinical superiority

Tumour control

Survival

Toxicity

Better quality of life / improved QALY's

OPTIONS AVAILABLE

Cost effectiveness

Real Option Analysis

Comparative effectiveness research

WHAT IS CER (IOM)?

The generation and synthesis of evidence that **compares** the benefits and harms of **alternative methods** to prevent/ diagnose/treat/ monitor a clinical condition or to improve the delivery of care in **real world** setting

Purpose: to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health care at both the individual and population levels

CER's distinguishing characteristics include informing a specific clinical or policy decision, **comparing** at least two approaches or interventions, describing results at the **subgroup** level, measuring benefits in **real-world** populations, and applying appropriate methods and data sources.

Source: Institute of Medicine. Initial National Priorities for Comparative Effectiveness Research, 2009.

MEASURING EFFICACY /EFFECTIVENESS

Health outcomes/endpoints (“benefits” and “harms”)

- mortality
- morbidity
- adverse events

Quality of life, also:

- functional status
- patient satisfaction

Intermediate (including surrogate*) endpoints

- e.g., blood pressure, lab values, EKG (“biomarkers”)

Accuracy of tests (screening, diagnosis, monitoring)

- sensitivity
- specificity
- predictive value positive, negative

* True surrogate: highly, reliably predictive of health outcomes

WHAT IS QUALITY OF LIFE?

WHO: “Health is not only the absence of infirmity and disease, but also a state of physical, mental and social well-being.”

Quality of Life: A multidimensional construct encompassing complete information on the impact of disease or its treatment on a patient’s usual or expected physical, psychological, and social well-being.

Fundamental Principle: QoL is assessed BY THE PATIENT

QUALITY OF LIFE ASSESSMENT CAN:-

Assist patient and doctor with decision making about treatments

Reveal benefits to patients despite objective toxicity

Evaluate different treatment outcomes

To be used to inform policy and resource allocation

Identify patients who might benefit from supportive interventions

Can be used as prognostic markers

HOW TO MEASURE QOL?

Generic instruments

Multi-item scales used across a wide-range of chronic-disease populations

Allow for comparisons of populations with different health conditions

Insensitive for effects of specific interventions

Cancer-specific instruments

Address problems specific to a population with cancer

Cancer type specific modules: sensitive and specific for clinically important QoL differences

Have been used in large series

INTERPRETATION AND APPLICATION OF HRQOL SCORES

Mean scores for a group can be compared with “normative values” for a sample of cancer patients

Changes in scores within a group can be assessed over time to determine effect of disease or treatment

Differences in scores can be compared between two groups given different treatments



QOL DATA

CNAO: PROTOCOL

Aims

To assess the impact of proton therapy on quality of life in adult chordoma and chondrosarcoma patients.

Protocol

Written consent from EORTC quality of life group

Validated questionnaire in Italian language

Timing: Pre-, Mid-, End-of-treatment, after 3mths, 6-9mths, 1year,

30 questions → ordinal scale



15 HRQOL parameters → continuous scale from 0-100

Fatigue Pain
Nausea and Vomiting
Dyspnea Appetite loss
Constipation Diarrhea
Financial difficulties
Insomnia

Physical functioning
Role functioning
Cognitive functioning
Emotional functioning
Social functioning

Global health status

Clinically important difference → 10 point difference (Osoba et al., 1998)

SCORING & INTERPRETATION EORTC QLQ C30 V.3.0

Multi-item and single item measures:

5 Functional scales

3 Symptom scales

1 Global health status

6 Single items

A high score represents a ***high level of functioning*** for Functional scale and a ***high Quality of life***, but ***high symptomatology*** for the Symptom scales.

Average of all items = Raw Score

Linear transformation of the Raw Score, so that all scores range from 0 to 100.

SOCIO- DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Age (years):

Mean SD: 49.5 16.4 years

Min- Max: 21- 73 years

Gender: 8M & 9F

Race: Caucasians

Site:

skull base : 65% (11)

sacral: 12% (2)

paraspinal: 18% (3)

paranasal sinuses: 5% (1)

Histology

chordoma: 77% (13)

chondrosarcoma: 23% (4)

SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS CONTD.....

Educational status:

All were literate with 30% (5)
having professional degrees

Marital status:

Living with a partner: 59% (10)
Living alone: 41% (7)

Occupational status:

Employed : 59% (10)
Unemployed: 12% (2)
Retired: 29% (5)

Children

Yes: 53% (9)
No: 47% (8)

Income level

Low: 17% (3)
Middle: 65% (11)
High: 17% (3)

TREATMENT PARAMETERS

Dose & fractionation

70 GyE/ 35 fr: 23%(4)

74 GyE/37 fr: 77% (13)

Total treatment time:

Mean 52.5 ± 4; 45-59 days

Previous radiotherapy

None

Number of surgeries

Average: 1, (0- 4)



**HOW SYMPTOMATIC WERE THE
PATIENTS IN THIS COHORT?**

**PHYSICIAN SCORED PRE-TREATMENT STATUS
(N= 17)**

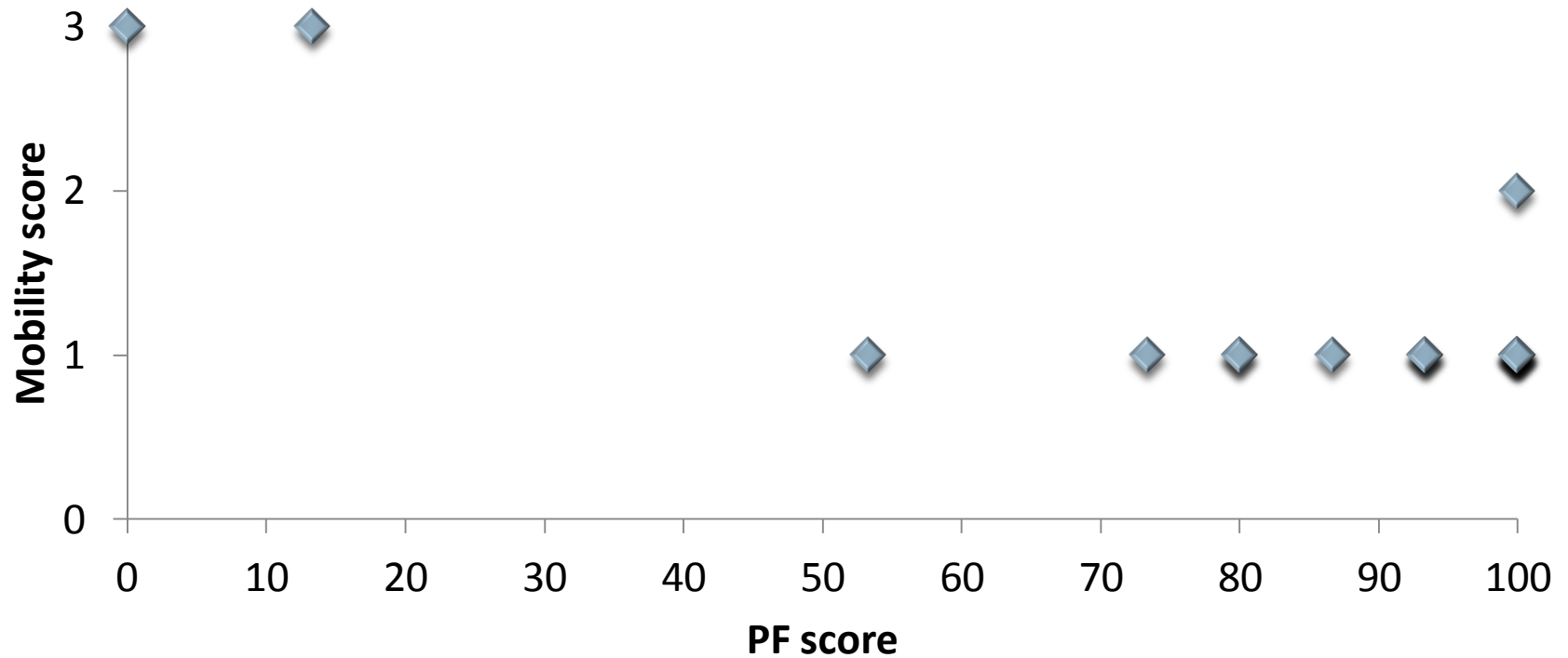
Parameter	No problem	Some problem	Severe limitation
Mobility	82% (14)	6% (1)	12% (2)
Self-care	82% (14)	6% (1)	12% (2)
Usual activity	76% (13)	12% (2)	12% (2)
Pain/discomfort	70% (12)	18% (3)	12% (2)
Anxiety/depression	59% (10)	29% (5)	12% (2)

PHYSICAL FUNCTIONING

	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a <u>long</u> walk?	1	2	3	4
3. Do you have any trouble taking a <u>short</u> walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

PHYSICIAN SCORES VS PATIENT SELF EVALUATED SCORES

Mobility vs Physical Functioning



QOL DATA: FUNCTIONAL SCORES

(MEAN ± SD, STATISTICAL DIFFERENCE)

	Pre-treatment	Mid-treatment	End-of-treatment	Statistical significance
Global Health status	71 ± 24.5	69.6 ± 18.6	68.1 ± 18.6	0.53
Physical functioning	80.3 ± 30.5	83.1 ± 23.4	81.2 ± 28.8	0.9
Role functioning	82.3 ± 29.7	84.3 ± 27.9	77.4 ± 32.2	0.1
Emotional functioning	77.4 ± 32.1	85.7 ± 20.9	85.7 ± 24.8	0.09
Cognitive functioning	84.3 ± 31.4	89.2 ± 25.6	88.2 ± 21.9	0.2
Social functioning	78.4 ± 34.7	78.4 ± 32.6	79.4 ± 30.4	0.7

GLOBAL HEALTH STATUS

29. How would you rate your overall health during the past week?

1 2 3 4 5 6 7

Very poor

Excellent

30. How would you rate your overall quality of life during the past week?

1 2 3 4 5 6 7

Very poor

Excellent

**CLINICAL IMPORTANT DIFFERENCE:
FUNCTIONAL OUTCOME
PRE-TREATMENT VS END-OF-TREATMENT**

	No change	Trivial (<4)	Small (4-10)		Medium/Clinically important difference (>10)	
			improvement	deterioration	improvement	deterioration
Global	6% (1)	0	12% (2)	24% (4)	24% (4)	35% (6)
Physical	29% (5)	0	18% (3)	24% (4)	18% (3)	12% (2)
Role	71% (12)	0	0	0	6% (1)	24% (4)
Emotional	47% (8)	0	18% (3)	6% (1)	24% (4)	6% (1)
Cognitive	77% (13)	0	0	0	17% (3)	6% (1)
Social	59% (10)	0	0	0	17% (3)	23% (4)

QOL DATA: SYMPTOM SCORES

(MEAN SD, STATISTICAL DIFFERENCE)

	Pre treatment	Mid treatment	End-of-treatment	Statistical significance
Fatigue	28.7 ± 30.4	18.3 ± 18.8	32.8 ± 30.9	0.4
Pain	10.7 ± 18.5	10.8 ± 17.6	11.7 ± 16.4	0.9
Sleep	27.4 ± 35.8	15.6 ± 23.9	19.6 ± 26.5	0.2
Financial difficulty	23.5 ± 28.3	33.3 ± 33.3	33.3 ± 33.3	0.2

CLINICALLY IMPORTANT DIFFERENCE: SYMPTOM SCORES

	No change	Trivial (<4)		Small (4-10)		Medium/Clinically important difference (>10)	
		improvement	deterioration	improvement	deterioration	improvement	deterioration
Fatigue	41% (7)	0	6% (1)	0	0	18% (3)	35% (6)
Pain	65% (11)	0	0	0	0	12% (2)	24% (4)
Sleep	41% (7)	0	0	0	0	35% (6)	24% (4)
Financial difficulty	65% (11)	0	0	0	0	12% (2)	24% (4)

CONCLUSION

At the very least, Quality of Life is not worsened at the end of a course of proton therapy treatment

Sample size is too small to demonstrate statistical significance

Longer follow-up is needed to document long term effects

Need to generate evidence to establish clinical superiority

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