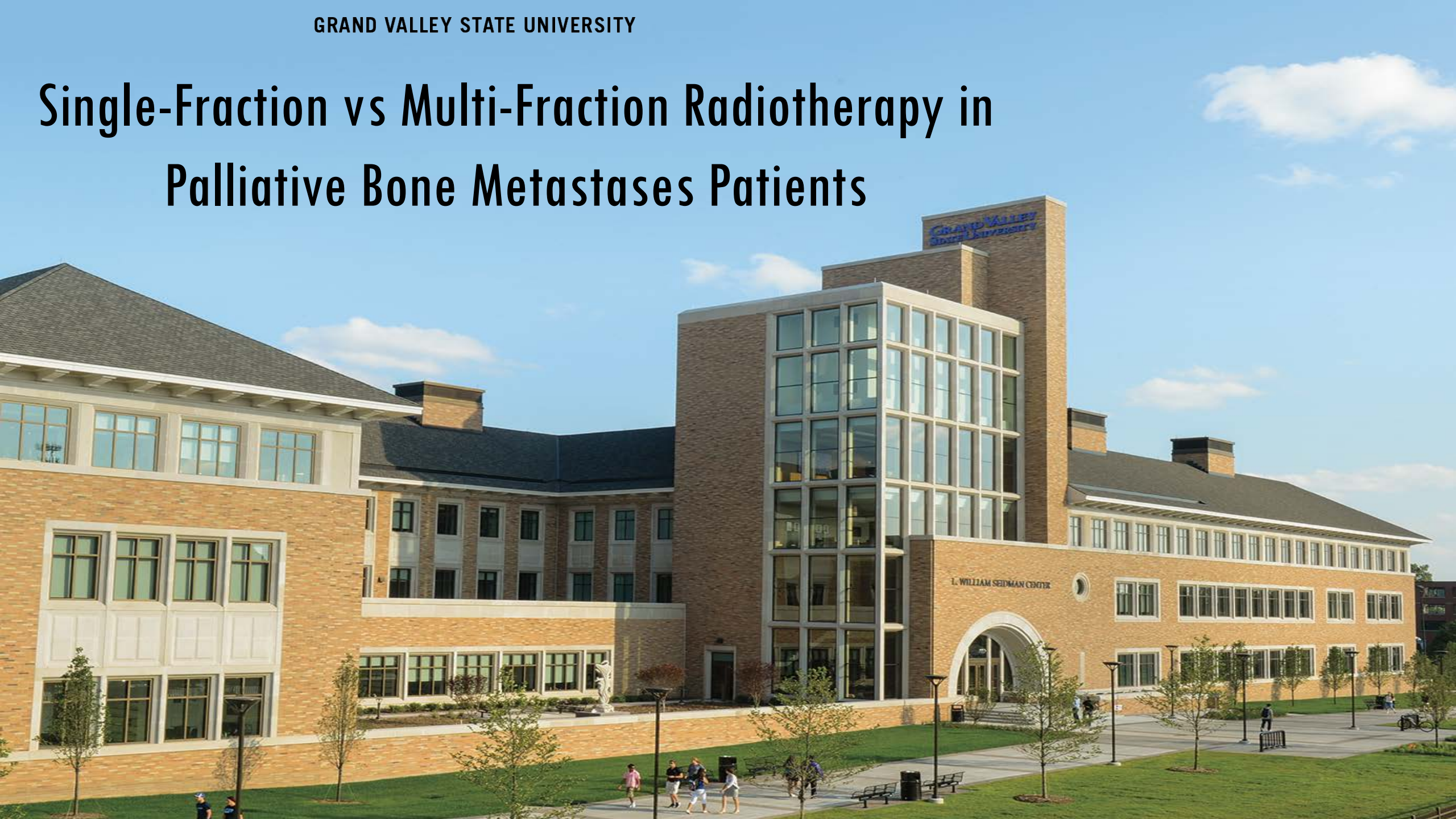
GRAND VALLEY STATE UNIVERSITY

Single-Fraction vs Multi-Fraction Radiotherapy in Palliative Bone Metastases Patients



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GVSU Academic Conference Fund ($500)

Overview

Introduction

Methods

Results

Discussion

Conclusion

Research Question

Is there a difference in the proportion of patients receiving single-fraction versus multi-fraction treatment based on:

- Primary Malignancy
- Age
- Gender
- Race
- Region
- Overall number of single versus multiple fraction treatments

Key issues- patterns of utilization

The Beginning

Why does this interest me?

https://www.spreadshirt.com/interesting+t-shirts?redirectFrom=en_GB&token=interesting+t-shirts

Background

What is bone metastases?

- *Lytic* lesions
  - Osteoclasts
    - Break down the bone
- *Blastic* lesions
  - Osteoblasts
    - Extra growth

http://www.meddean.luc.edu/lumen/meded/radio/curriculum/surgery/met_bone_list1.htm

30-70% of cancer patients

Background

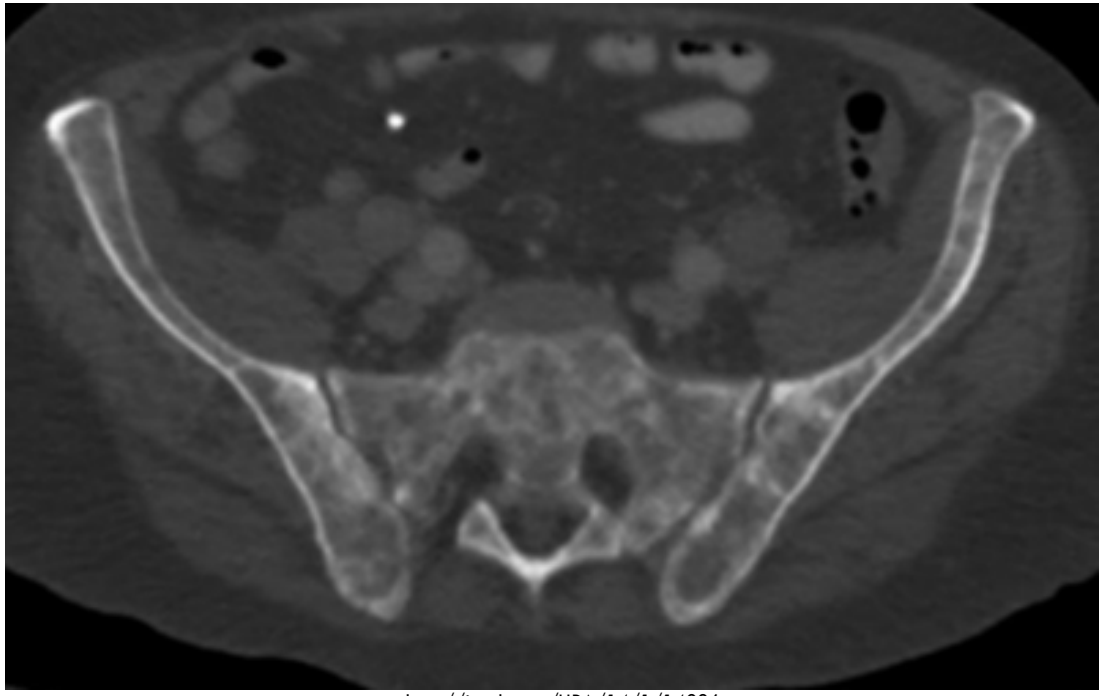
What do we treat?

- Multiple metastases
- CTV defined by pain & local tenderness (not radiological extent)

Background

Symptoms

- Severe pain
- Spinal cord compression
- Hypercalcemia
- Pathologic fracture



http://ispub.com/IJRA/14/1/14086

What does Radiation do?

- Clinically relevant outcome = control pain → Quality of Life

Background

Median Survival= < 1 year

Other treatment options

- Pharmacological interventions
- Chemotherapy
- Radiopharmaceuticals

Background

RT is effective: within 1-4 weeks post RT

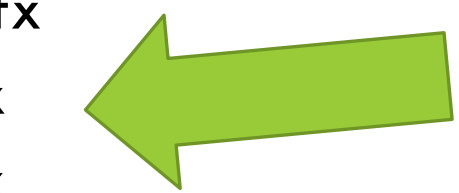
Partial Pain Relief: 60-80%

Complete Pain Relief: 30-50%

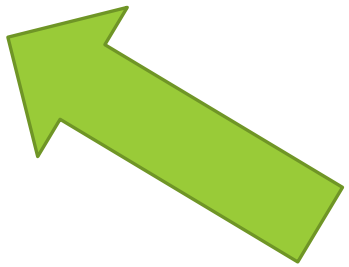
Background

Common fractionations:

- 30 Gy in 10 fx
- 24 Gy in 6 fx
- 20 Gy in 5 fx
- 8 Gy in 1 fx



Multi-Fraction



Single-Fraction

Introduction

ASTRO Guidelines:

- Guidelines Subcommittee of the Clinical Affairs and Quality Committee of the ASTRO
- Provides guidance on the use of palliative RT for bone metastases to patients & physicians

Introduction

ASTRO Guidelines:

- Systemic Literature Review
  - "Radiotherapy bone metastases"
  - PubMed: 1998 - 2009
    - 4,287 articles
      - 25 randomized clinical trials, 20 prospective single-arm studies & 4 meta-analyses/systematic reviews

Introduction

ASTRO Guidelines:

- Most patients 8 Gy in 1 fraction is a safe and effective treatment
  - Shorter acute radiation side effects
  - Retreatment rate: 8% versus 20%
  - Pain relief similar

Conclude that the US has shown a delay and suggests that a change in the dose regimen should occur.

Introduction

Multi-fraction Should be Considered in:

- Spinal cord compression, cauda equine compression or radicular pain
- Previous treatment to the spine
- Femoral axial cortical involvement > 3cm in length
- Surgical stabilization
- Retreatment would be problematic

Introduction

International

- Canada
  - 20 Gy in 5 fx
- United Kingdom
- Western Europe
- Australia
- New Zealand
- India

All more likely to prescribe a single fraction

Population

Retrospective study based on billing data

Research Data Assistance Center (ResDAC)

- Outpatient Medicare beneficiaries in 2014
  - Outpatient Limited Data Sets (LDS) and the Denominator file (which includes the demographic data)
  - 5% random selection from the total Medicare population = roughly 2.8 million beneficiaries (from the 55 million)

Population

- Medicare eligibility includes beneficiaries:
  - 65 or older
  - Permanently disabled
  - End-stage renal disease
  - Lou Gehrig's disease.

Population

Data

- Final action, fee-for-service claims
- Medical institutional provider numbers
- Physician identifiers
- Ninth Revision (ICD-9) diagnosis codes
- HCPCS codes
- Dates of service
- Reimbursement amount
- Outpatient provider number
- Revenue center codes
- Beneficiary demographic information

Population

Outpatient Providers

- Hospital outpatient departments
- Rural health clinics
- Renal dialysis facilities
- Outpatient rehabilitation facilities
- Community mental health centers

Ethical Considerations

Data Use Agreement (DUA)

- Outlines the purpose, project methods, data management safeguards, key personnel and dissemination of the data but does not go through a privacy board review

Beneficiary level PHI, but exclude specified direct identifiers.

- Some variables are encrypted, blanked or ranged to ensure privacy.
  - IRB approval was not required

Population

Roughly 2.8 million beneficiaries

- Diagnosis and RT billing codes
- Current Procedural Terminology (CPT)

Steps:

- 1) Diagnosis code 198.5: secondary malignant neoplasm of bone and bone marrow (5,987)
- 2) RT delivery CPT code: 77401-77416 (392 beneficiaries)
- 3) Exclusions: complicated treatments, brachytherapy treatments, or ≥ 16 fractions
- 4) CPT codes 77401-77416 counted to determine the number of fractions delivered

Population

The final sample population: **303 beneficiaries**

- 50 beneficiaries that were missing a primary malignancy diagnosis code

Is there a difference in the proportion of patients receiving single-fraction versus multi-fraction treatment based on:

- Primary Malignancy
- Age
- Gender
- Race
- Region

Groupings

Primary Malignancy
- Breast
- Prostate
- Lung
- Kidney
- Thyroid
- Melanoma
- Other or Multiple

Age Group
- Under 65
- 65 to 75
- 76 to 85
- Over 85

Gender
- Male
- Female

Race
- White
- Black
- Asian
- Hispanic
- North American Native
- Other
- Unknown

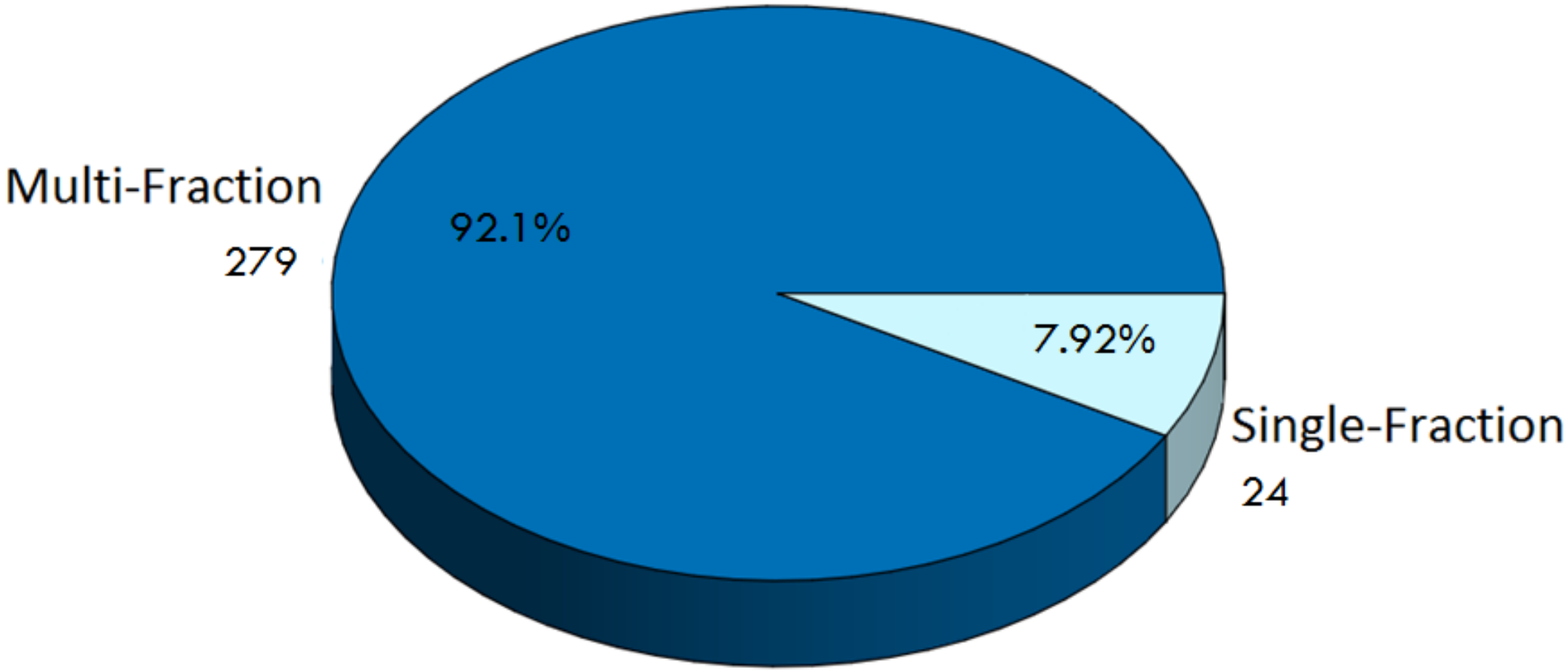
Geographic Region
- Northeast
- Southeast
- Midwest
- Southwest
- West

Methods

Statistics

- Chi-square test was done for each variable (primary malignancy, gender, race, region and age)
  - Fisher's test when assumptions were not met
  - Significance level = 0.05

Results



Results: Total Population

Primary Malignancy

- Lung most common (*n*=67; 26.5%)
  - Followed by Prostate (*n*=55; 21.7%) and Breast (*n*=49; 19.4%)

Age

- Majority were 65-75 years (*n*=129; 42.6%) and 76-85 years (*n*=106; 35%)

Gender

- Slightly more males than females

Results: Total Population

Race

- Majority were Caucasian (*n*=276; 91.1%)

Geographic Region

- Majority in the Southeast (*n*=123; 40.6%)

Results: Single-Fraction

- Primary Malignancy
  - Lung most common lung (*n*=10; 55.6%)
  - Prostate (*n*=3; 16.7%)
  - Kidney (*n*=2; 11.1%)
- Age
  - Mean age = 74.5 years
  - Most common age group 76-85 (*n*=12; 50%)
  - 65-75 year olds (*n* =8; 33.3%)
- Gender
  - Equal

Results: Single-Fraction

Race

- All were Caucasian (*n*=24; 100%)

Geographic Region

- Majority in the Southeast (*n*=12; 50%)

Results: Multi-Fraction

Primary Malignancy

- Lung most common lung (*n*=57; 24.3%)
- Prostate (*n*=52; 22.1%)
- Breast (*n*=48; 20.4%)

Age

- Mean age = 73.6 years
- Majority were 65-75 years of age (*n*=121: 43.4%)
- 76-85 year olds (*n*=94; 33.7%)

Gender

- Equal

Results: Multi-Fraction

Race

- Majority were Caucasian (*n*=252; 90.3%)

Geographic Region

- Majority in the Southeast (*n*=111; 39.8%)

Results

Table 2
Chi-square and Fisher's exact test.

Variable	Test Statistic	*p* value
Gender	0.0141	0.9055
Primary Malignancy	n/a	0.0759
Race	n/a	0.67
Region	n/a	0.8239
Age Group	n/a	0.3688

Results

Fisher's exact test separated by gender for Primary Malignancy.

	Gender	Primary Malignancy	Fractions Less than 10	10	More than 10
		Kidney	4 (33.3)	5 (41.7)	3 (25)
$p = 0.5722$	Male	Lung	18 (50)	10 (27.8)	8 (22.2)
		Prostate	20 (36.4)	16 (29.1)	19 (34.6)
		Kidney	2 (28.6)	3 (42.9)	2 (28.6)
$p = 0.5009$	Female	Lung	17 (54.8)	10 (32.3)	4 (12.9)
		Breast	19 (38.8)	18 (36.7)	12 (24.5)

Not significant

Single Fraction Rate

Single-fraction rate = 7.92%

- No significant changes have been made since the recommendations were published in 2011.

Top three primary diagnoses:

- Lung 26.5%
- Prostate 21.7%
- Breast 19.4%

- Matches current literature

Race

Race

- According to the Kaiser Family Foundation, in 2014
  - 76% white
  - 10% black
  - 8% Hispanic
  - 5% were Other.

- Compared to 91.1%

Retreatments

Retreatments

- 8% versus 20%
- Actual reason for retreatment is often not clear
- 4-6 weeks post RT
- Feasible, safe & effective
  - No conclusive statement on dosing & fractionation
  - Recent trial: re-irradiation to a previously treated skeletal site of bone pain can provide pain relief in 50% of patients

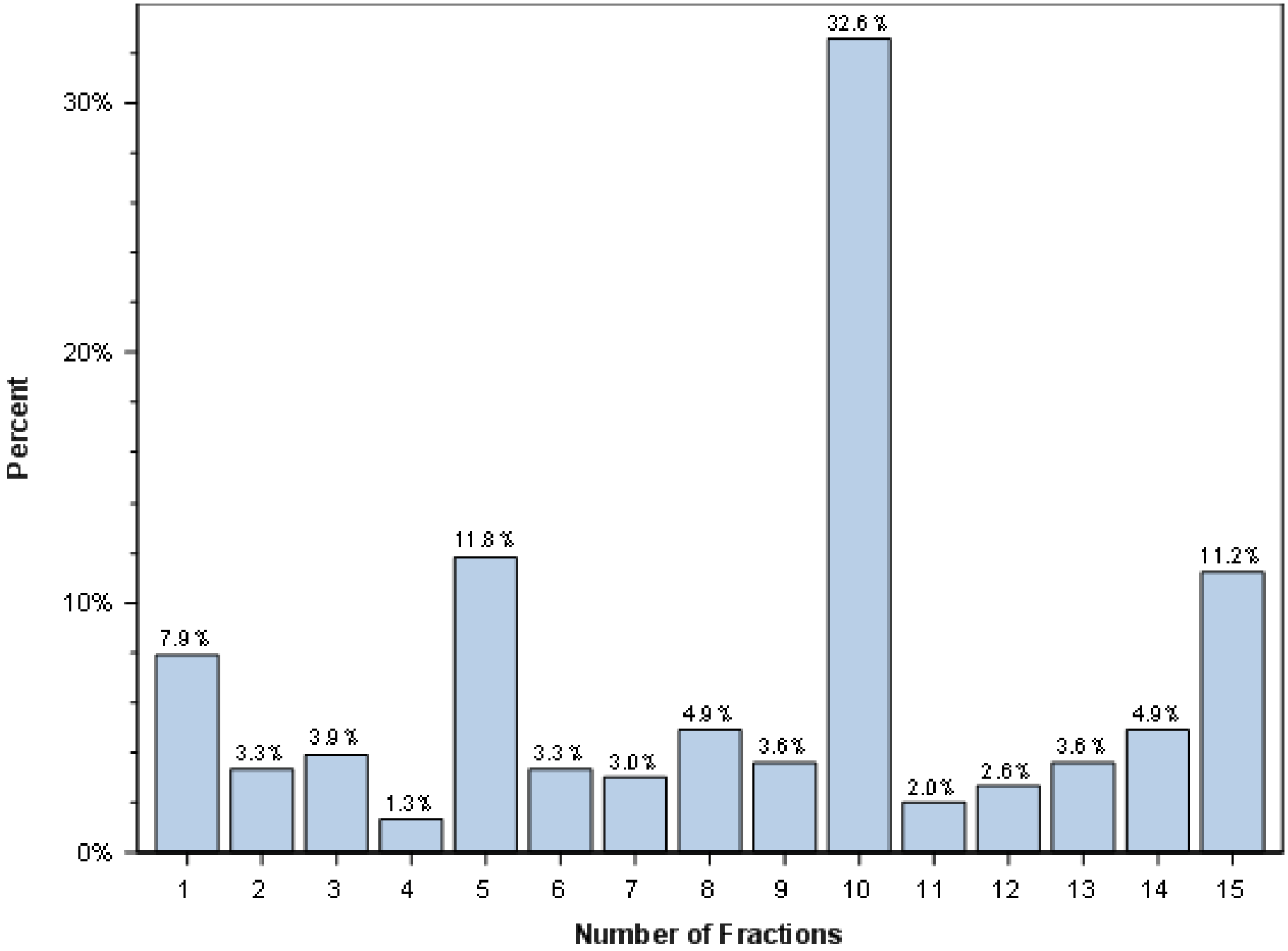
Retreatments

Patient and physician choice and bias

Price *et al.*

- More likely with 8 Gy/1fx schedule
- Increased painkiller use in 30 Gy /10 fx

Fractions


Percent
30%
20%
10%
0%
7.9%
3.3%
3.9%
1.3%
11.8%
3.3%
3.0%
4.9%
3.6%
32.6%
2.0%
2.6%
3.6%
4.9%
11.2%
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
Number of Fractions

Long Term Side Effects

Task Group: no unacceptable rates of long term side effects

- Statistically insignificant or *clinically* insignificant
  - Example: Pathological fracture rate – small percentage but significant
    - 2004 Study: 1.6% vs 3%

- RTOG 97-14: spinal cord myelopathy
  - Re-evaluated: 0% risk

Palliative Radiation Objective

JAMA in 1964

"Overall treatment time must be short. Cost must be minimized. Convenience of treatment must be considered."

Distinction between curative and palliative goals has become blurred

Prognosis

Overestimate survival by a factor of 3 or more

Prognostic tools

Shorter life expectancy:

- Patient: poor performance status, advanced age, significant weight loss, severe comorbid disease
- Cancer: metastatic disease, aggressive histology
- Treatment: poor response to systemic therapy, previous radiotherapy

Prognosis

Karnofsky Performance Status

100	Normal; no complaints; no evidence of disease
90	Able to carry on normal activity; minor signs or symptoms of disease
80	Normal activity with effort; some signs or symptoms of disease
70	Cares for self; unable to carry on normal activity or to do active work
60	Requires occasional assistance but is able to care for most personal needs
50	Requires considerable assistance and frequent medical care
40	Disabled; requires special care and assistance
30	Severely disabled; hospitalisation is indicated, although death not imminent
20	Very sick; hospitalisation necessary; active support treatment is necessary
10	Moribund; fatal processes
0	Dead

http://cancergrace.org/cancer-101/files/2015/07/Karnofsky-Performance-Status-PS-Scale.gif

Prognosis

The selection of palliative radiotherapy dose depends not only on prognosis but also on:

- performance status
- comorbidities
- risk of acute toxicity
- prior treatment
- delivery of systemic therapy
- patient wishes

Hospice

Barriers

- Cost of treatment
- Transportation difficulties
- Short patient life expectancy
- Educational lapses between the specialties

3% of hospice patients receive radiation therapy

- cancer is the most common diagnosis in patients admitted to hospice

Hospice

The disparity between radiotherapy costs and the hospice per diem of about $120 per day was limiting

Perceived unwillingness of radiation oncologists to offer single-fraction treatment to eligible patients with painful bone metastases.

Barriers & Limitations

Education	No formal palliative care training. Minimal protected time at national meetings for palliative oncology
Research	Lack of federal funds dedicated to end-of-life studies
Financial	Increasing radiotherapy costs due to technological advances

National Hospice and Palliative Care Organization

Limitations

Limitations

- Difficulty in finding data
- Large data in multiple files
  - SAS code on a standard PC -upwards of 40 minutes
    - Blade Server from the Engineering department – roughly 2-3 minutes
- CPT codes were under HCPCS column

Inexperience

Limitations

By hand review 303 beneficiaries treatments & count the number of fractions.

Table of HCPCS_CD by date_diff							
HCPCS_CD	date_diff						
Frequency	0	1	4	5	6	7	Total
77416	1	1	1	1	1	1	6
Total	1	1	1	1	1	1	6

Limitations

- No prescribing information (multiple courses)
- Not generalizable
- Only outpatient data
- Unable to determine if met the criteria for single-fraction

Take Away…

Criteria for Palliation of Bone Metastases – Clinical Applications - 2007

There is therefore overwhelming clinical trial evidence to show that a single dose of 8 Gy is adequate and for palliation optimal for the patient with localized metastatic bone pain. There is no role for multifraction treatment in uncomplicated bone metastasis.

Take Away…

No significant results

- Demographic data or primary malignancy was not associated with the prescribing habits
- Current prescribing practices

Roughly 41% of the population died within 2014

Take Away…

Always ask questions.

Continue to learn.

Have a good professional rapport with your physician.

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