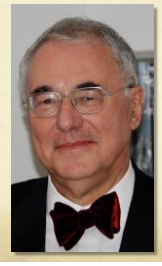
In Memoriam of Michael Goitein



In Memoriam of Michael Goitein

MGH 1988

In Memoriam of Michael Goitein

Michael's 70th birthday - PSI, Switzerland, 2009

In Memoriam of Michael Goitein

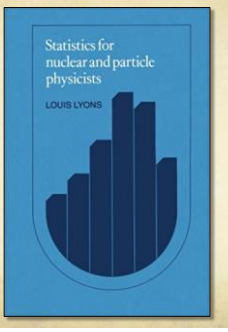
Michael's 70th birthday - Windisch, Switzerland, 2009

OBITUARY

Michael Goitein, 1939-2016: A Giant of Modern Medical Physics

Herman Suit, MD DPhil,* George Chen, PhD,† Thomas Bortfeld, PhD,* Alfred Smith, PhD,† Jay Loeffler, MD,* Edward Epp, PhD,† Andrzej Niemierko, PhD,* and Gudrun Goitein, MD‡

"Michael was struck by the fact that uncertainty analysis and error bars .... were virtually absent in medical physics."



OBITUARY

Michael Goitein, 1939-2016: A Giant of Modern Medical Physics

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"He considered not only the science of the developments he led but also their ethical implications."

"It's unethical to carry out bad scientific experiments. However praiseworthy a study may be from other point of view, if the statistical aspects are substandard then the research is unethical."

D.G.Altman, "Statistics and ethics in medical research", in *Statistics in Practice* (British Med. Assn., London, 1982) pp. 1-21.

"The combination of some data and an aching desire for an answer does not ensure that a reasonable answer can be extracted from a given body of data."

John Tukey (1986), "Sunset salvo". *The American Statistician*, 40(1).

"If you torture your data long enough, they will tell you whatever you want to hear."

Mills, J. L. 1993. Data torturing. *New England Journal of Medicine* 329, (16): 1196.

"The problem of poor research documentation and statistical reporting in the biomedical literature is long-standing, world-wide, pervasive, potentially serious, and not at all apparent to many readers."

Schor S, Karten I. *Statistical evaluation of medical journal manuscripts*. JAMA. 1966;195:1123-8.

"These reviews [of statistical errors] reveal a remarkable and depressing consistency, with typically around 50% of reviewed papers being found to contain clear statistical errors. A large portion of these errors are so great as to cast doubts on the validity of the paper's conclusions."

Yancy JM. *Ten rules for reading clinical research reports [Editorial]*. Br J Surg. 1990;159:553-9.

"Half of published research is in fact unreliable at best, if not completely false"

Richard Horton, Editor-in Chief of *the Lancet*.
Vol 385, April 11, 2015.

"Much of the scientific literature, perhaps half, may simply be untrue. Afflicted by studies with small sample sizes, tiny effects, invalid exploratory analyses, and flagrant conflicts of interest, together with an obsession for pursuing fashionable trends of dubious importance, science has taken a turn towards darkness.

Richard Horton, Editor-in Chief of *the Lancet*.
Vol 385, April 11, 2015.

"It is simply no longer possible to believe much of the clinical research that is published, or to rely on the judgment of trusted physicians or authoritative medical guidelines. I take no pleasure in this conclusion, which I reached slowly and reluctantly over my two decades as an editor of the New England Journal of Medicine"

Marcia Angell MD, Editor-in Chief of *the NEJM, 2010*.
(first woman to have served as Editor-in-Chief of the journal since it was founded in 1812)

Analysis of clinical outcomes

1. Table of patient and treatment characteristics

⬇

2. Univariate analysis

⬇

3. Multivariate analysis

(variable selection based on p values from univariate analysis)

1. Table of patient and treatment characteristics

Factor	Value
N	1000
Modality	
Proton	481 (48.1%)
IMRT	519 (51.9%)
Stage	
Stage I	513 (51.3%)
Stage II	487 (48.7%)
Age, mean (SD)	41 (7)
Local Control	
No	383 (38.3%)
Yes	617 (61.7%)

2. Univariate analysis (modality)

Modality	Local Control: No	Local Control: Yes	Total
Proton	178	303	481
	37.01	62.99	100.00
IMRT	205	314	519
	39.50	60.50	100.00
Total	383	617	1,000
	38.30	61.70	100.00

Pearson chi2(1) = 0.6565 P = 0.418

2. Univariate analysis (stage)

Stage	Local Control: No	Yes	Total
Stage I	183	330	513
	35.67	64.33	100.00
Stage II	200	287	487
	41.07	58.93	100.00
Total	383	617	1,000
	38.30	61.70	100.00

Pearson chi2(1) = 3.0774 P = 0.079

2. Univariate analysis (age)

Logistic regression — Number of obs = 1,000; LR chi2(1) = 6.19; Prob > chi2 = 0.0129; Log likelihood = -662.41893; Pseudo R2 = 0.0047

outcome	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Age	.9771805	.0091013	-2.48	0.013	.9595041	.9951825
_cons	4.163152	1.622735	3.66	0.000	1.939263	8.937333

3. Multivariate analysis

Logistic regression — Number of obs = 1,000; LR chi2(2) = 7.77; Prob > chi2 = 0.0205; Log likelihood = -661.62687; Pseudo R2 = 0.0058

outcome	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Stage	.8453733	.1128303	-1.26	0.208	.6507893	1.098137
Age	.9796212	.0093356	-2.16	0.031	.9614935	.9980907
_cons	4.081972	1.594108	3.60	0.000	1.898696	8.775757

3. Multivariate analysis

Logistic regression — Number of obs = 1,000; LR chi2(3) = 12.65; Prob > chi2 = 0.0055; Log likelihood = -659.19032; Pseudo R2 = 0.0095

outcome	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Modality	.6108293	.1375534	-2.19	0.029	.392859	.9497361
Stage	.5694603	.1284304	-2.50	0.013	.3660092	.8860024
Age	.9920646	.0110427	-0.72	0.474	.9706556	1.013946
_cons	3.817514	1.502867	3.40	0.001	1.764746	8.258079

3. Multivariate analysis

Model 1	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Stage	.8453733	.1128303	-1.26	0.208	.6507893	1.098137
Age	.9796212	.0093356	-2.16	0.031	.9614935	.9980907
_cons	4.081972	1.594108	3.60	0.000	1.898696	8.775757

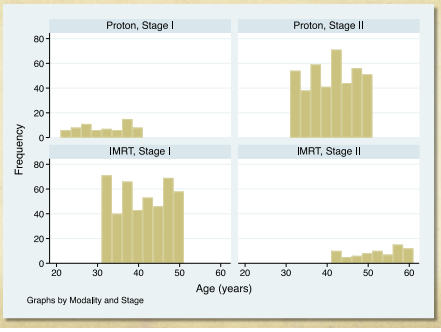
Model 2	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Modality	.6108293	.1375534	-2.19	0.029	.392859	.9497361
Stage	.5694603	.1284304	-2.50	0.013	.3660092	.8860024
Age	.9920646	.0110427	-0.72	0.474	.9706556	1.013946
_cons	3.817514	1.502867	3.40	0.001	1.764746	8.258079

3. Multivariate analysis

Model 3	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
Modality	.5626285	.1091502	-2.96	0.003	.38467	.8229155
Stage	.5240989	.1015535	-3.33	0.001	.3584906	.7662116
_cons	2.991784	.5872344	5.58	0.000	2.036359	4.395478

The Truth (model used to generate data - 1000 cases):

	Odds Ratio	Probabilities of local control	True	Data-estimated
Modality	.65	IMRT Stage II	51%	47% (95%CI: 42-60%)
Stage	.60	IMRT Stage I	62%	61% (95%CI: 57-66%)
Age	1.0	Protons Stage II	64%	63% (95%CI: 59-68%)
		Protons Stage I	73%	75% (95%CI: 65-80%)



Closing remarks