DEVELOPMENT OF A NOMOGRAM TO PREDICT GRADE 2-3 ACUTE GI TOXICITY (RTOG/EORTC) FOR PROSTATE CANCER 3D-CRT

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PROSTATE CANCER:
PREVISIONAL MODELLINGS IN RADIATION ONCOLOGY

AIMED AT :

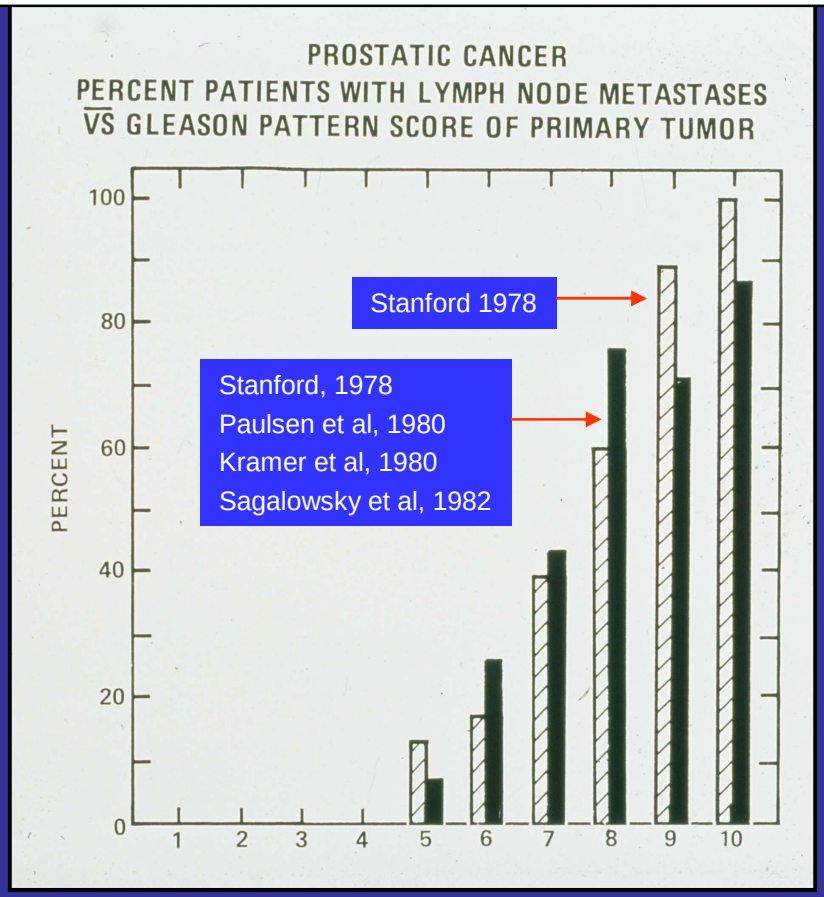
1. PREDICTING SPECIFIC PATHOLOGICAL FEATURES (LNI, ECE, SVI)
2. PREDICTING SPECIFIC CLINICAL END POINTS REGARDING TREATMENT RESULTS (bNED, DM, DFS, OS, PCM)

ADRESSED TO:

1. COUNSEL PATIENTS
2. HELP SELECTING ANATOMICAL TARGET(S) FOR RADIATION
3. HELP SELECTING RADIATION DOSE LEVELS
4. HELP SELECTING COMBO THERAPY IN STANDARD AND RESEARCH TRIALS

THE FIRST PREDICTIVE MODEL IN PROSTATE CANCER: DEVELOPED FOR THE RADIATION DECISION-MAKING PROCESS (PELVIS XRT: y/n)

S. Woo, I. Kaplan, M. Roach, M. Bagshaw, FORMULA TO ESTIMATE RISK OF PELVIC LYMPH NODE METASTASIS FROM THE TOTAL GLEASON SCORE, J Urol, 1988



PROSTATE CANCER:
PREDICTIVE MODELLING IN RADIATION ONCOLOGY

MEDLINE SEARCH FROM 1980 TO SEPTEMBER 2006 : prostate cancer, radiation therapy, brachytherapy, nomogram, algorithm, genetic algorithm, prediction, predictive model, ANN, propensity scoring, Bayesian NN

17 MODELS FOUND FOR EBRT (AND 3 FOR BCT) :

15/17 PREDICTING CLINICAL RESULTS
1 DEALING ALSO WITH TOX PREVISION
2/17 PREDICTING LIFE EXPECTANCY

EXPRESSED AS PROBABILITY FORMULAS, PROBABILITY GRAPHS, PROBABILITY TABLES, NOMOGRAMS, RISK CLASSES AND DEVELOPED USING FROM CLASSICAL STATISTICAL METHODS TO ANN, GENETIC ALGORITHMS AND PROPENSITY SCORING

PROSTATE CANCER:
PREDICTIVE MODELLING IN RADIATION ONCOLOGY

CURIOUSLY, ONLY ONE MODEL (ANN) FACES THE ISSUE OF THE PREVISION OF TREATMENT SIDE EFFECTS
(Gulliford et al, Radiother Oncol, 2004)

BUT NO PRACTICAL TOOL IS AVAILABLE

UROLOGISTS DEVELOPED ONLY TWO PREVISIONAL MODELS ON TOXICITY, PREDICTING:

1. THE PROBABILITY OF PERI-OP MORTALITY
(Tewari et al., Clinical Prostate Cancer, 2004)
2. THE PROBABILITY OF HOMOLOGOUS TRANSFUSION
(A. Dash et al, Urology, 2004)

PURPOSE

TO TRY TO PREDICT MODERATE/SEVERE RTOG/EORTC ACUTE LGI TOXICITY IN PROSTATE CANCER PATIENTS UNDERGOING 3D-CRT,

USING A DEVICE (NOMOGRAM) WHICH TAKES INTO ACCOUNT CLINICAL AND DOSIMETRIC VARIABLES PROVED TO BE STATISTICALLY SIGNIFICANT IN THE AIROPROS 0102 TRIAL

METHODS AND MATERIALS

PATIENT CHARACTERISTICS

- 1132 PATIENTS ACCRUED (July 2002 – March 2004, 22 Centers)
- **99.3% of patients are available for grade 2-3 LGI toxicity analysis**
- TOTAL DOSE: PROSTATE 70-80 Gy (mean 74.4 Gy)
  PELVIS 40-50 Gy (mean 46.8 Gy)
- DOSE PER FRACTION 1.8-2.0 Gy

POTENTIAL BIASES (CONTOURING, RECTAL LENGTH DEFINITION, etc) CONTROLLED BY RIGID PRE-TREATMENT RECOMMENDATIONS (PREVIOUSLY SHARED WITH TRIAL PARTECIPANTS)

METHODS AND MATERIALS

- **VARIABLES ANALYZED:**
  MEAN/MAX RECTAL DOSE, ICRU DOSE, PELVIC XRT, PRE-TREATMENT GI MORBIDITIES, HORMONAL THERAPY, DIABETES, HYPERTENSION, DRUG PRESCRIPTION

- **STATISTICAL ANALYSIS:**
  - UNI AND MULTIVARIATE LOGISTIC ANALYSES

- **NOMOGRAM DEVELOPED USING THE R-PROJECT SOFTWARE (www.r-project.org)**

RESULTS

GRADE ≥ 2 RECTAL TOX (25.9 %)

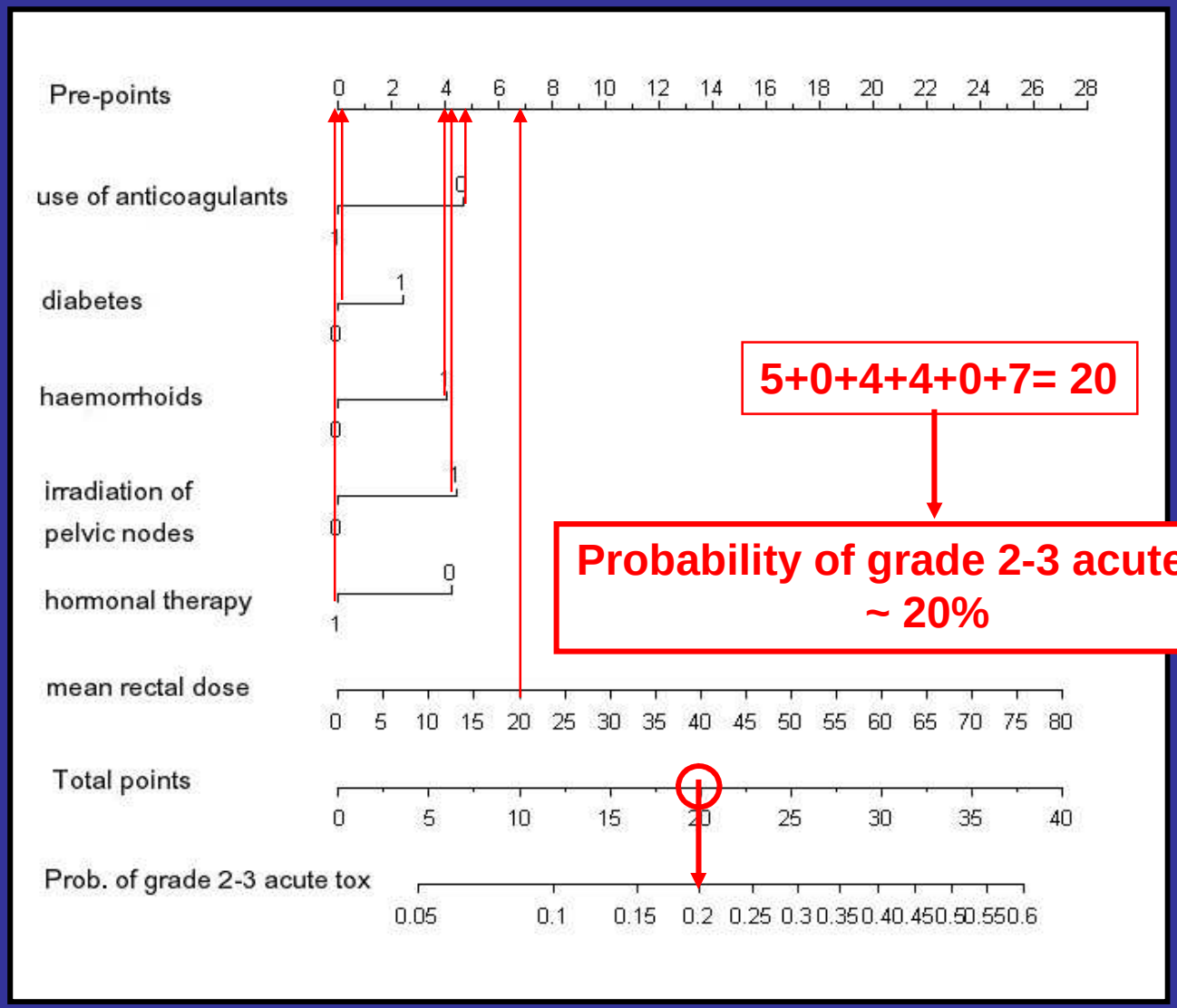
(MODIFIED RTOG/EORTC SCORING SYSTEM)

	univariate analysis			MVA	
	p value	Inc. % no	Inc. % yes	p value	OR
HAEMORRHOIDS	0,08	25,0	30,6	**0,02**	1,51
ANTICOAGULANTS	0,02	27,6	20,2	**0,02**	0,63
DIABETES	0,07	25,3	34,0	0,34	1,28
AD	0,06	31,9	24,4	**0,04**	0,65
PELVIC XRT	0,04	25,4	36,9	0,11	1,56
MEAN RECTAL DOSE *	0,02	22,0	29,9	**0,0004**	1,035

** median stratified, median value=51 Gy*

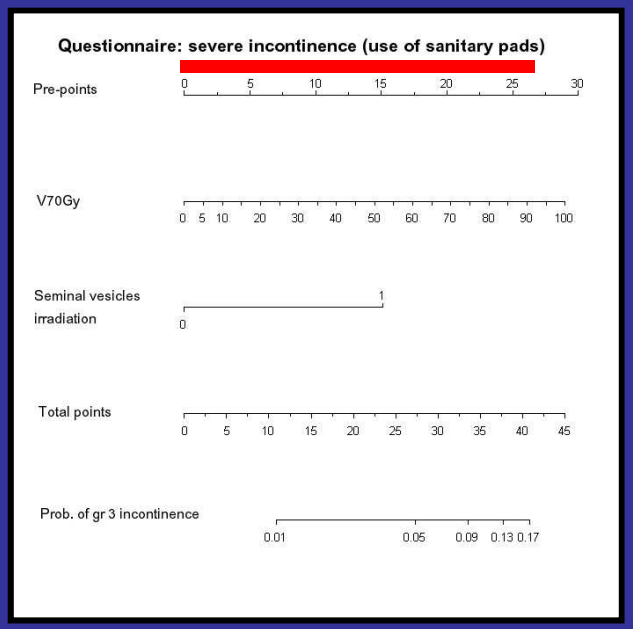
1. In multivariate analysis, mean rectal dose, haemorrhoids, anticoagulants and AD are highly correlated with toxicity.
2. Diabetes and pelvic node irradiation maintain a role in predicting rectal toxicity.
3. Anticoagulants and AD are protective, while the other factors increase the risk of rectal side effects.

AIROPROS 0102 NOMOGRAM :
PREDICTION OF GRADE ≥ 2 ACUTE RECTAL TOXICITY (RTOG/EORTC SCORING)

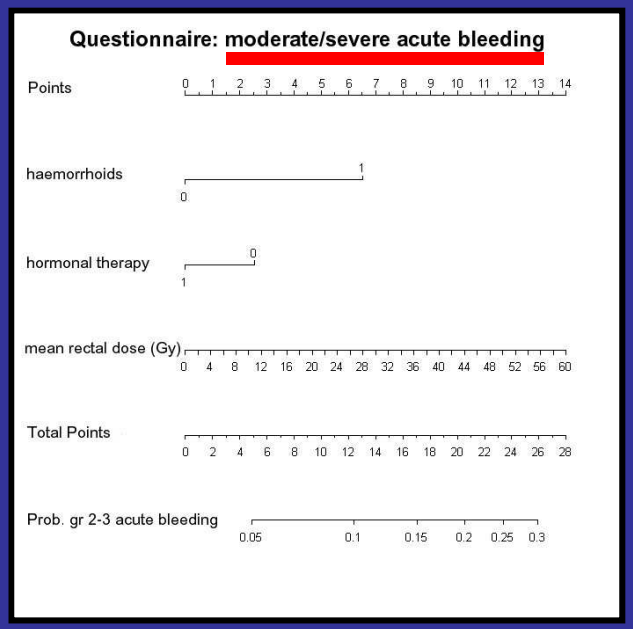


PREDICTING TOXICITY : WORK IN PROGRESS

1. NOMOGRAM VALIDATION
2. DEVELOPMENT OF NEW NOMOGRAMS FOR ACUTE RECTAL SYNDROME (SOMA-LENT SCALE)



Valdagni and Rancati, unpublished, July 2006



3. DEVELOPMENT OF NOMOGRAMS FOR LATE RECTAL SYNDROME (SOMA-LENT SCALE)

CONCLUSION

NOMOGRAMS EVALUATE THE COMBINED EFFECTS OF MULTIPLE INDEPENDENT FACTORS FOUND TO BE PROGNOSTICALLY VALUABLE FOR A SPECIFIC DISEASE. IN THIS WAY NOMOGRAMS EVALUATE A PATIENT'S CLINICAL PARAMETERS AND PROVIDE A TAILORED PROBABILITY OF A PARTICULAR OUTCOME

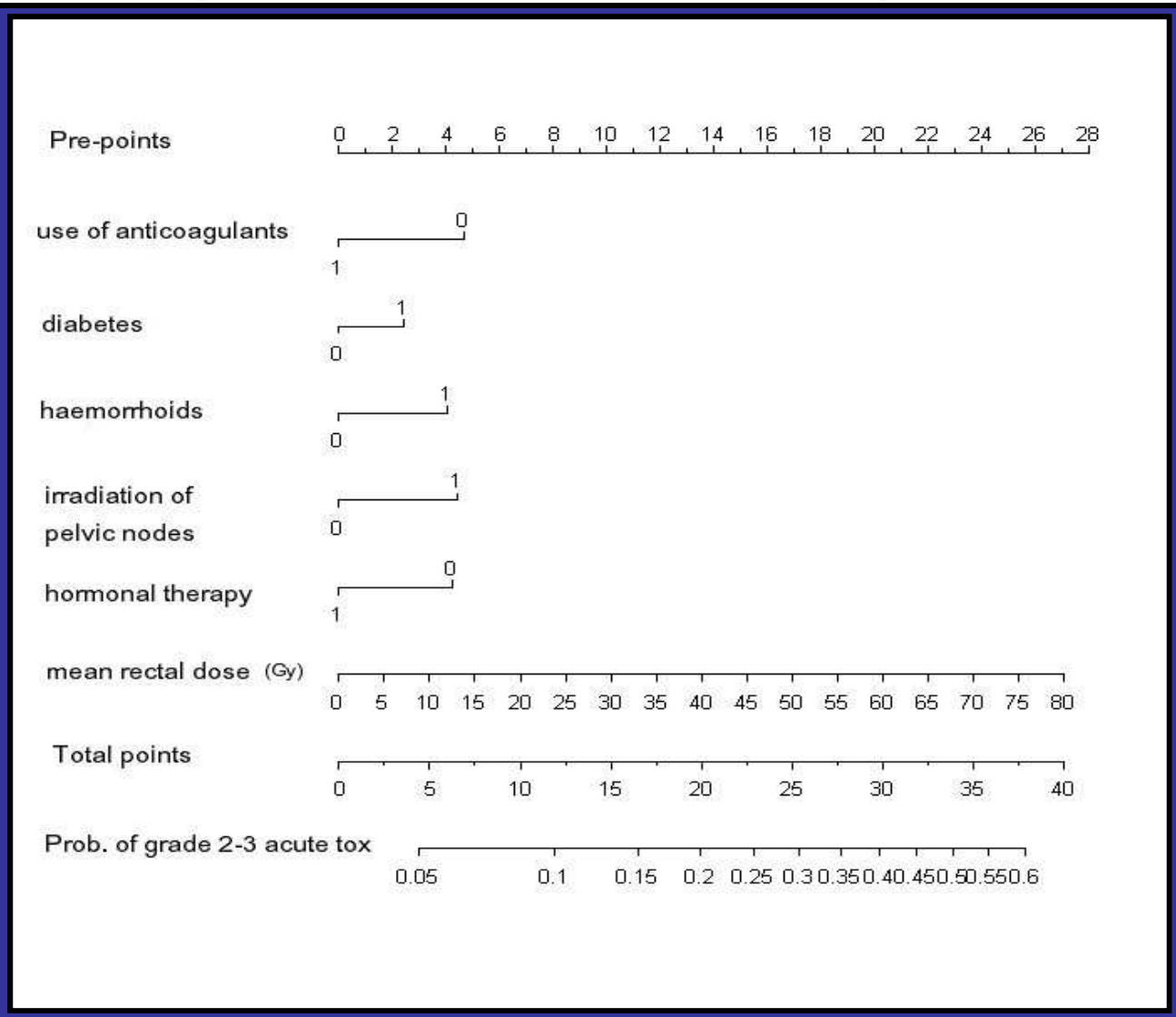
GRADE 2-3 ACUTE TOXICITIES OCCUR IN ~25% OF PATIENTS

EVIDENCE IS MOUNTING THAT ACUTE DAMAGE PLAYS A SIGNIFICANT ROLE ON LATE TOXICITY (i.e. Dutch Trial, IJROBP 2006)

OUR NOMOGRAM IS THE FIRST ATTEMPT TO HELP CLINICIANS PREDICT MODERATE / SEVERE ACUTE TOXICITY USING DOSIMETRIC AS WELL AS CLINICAL VARIABLES. IF VALIDATED, THIS TOOL MIGHT BE USEFUL TO OPTIMIZE TREATMENT STRATEGY IN EVERY SINGLE PATIENT

The AIRO PROS 0102 trial was partially supported by a Fondazione Italo Monzino grant

AIROPROS 0102 NOMOGRAM : PREDICTION OF GRADE ≥ 2 ACUTE RECTAL TOXICITY (RTOG/EORTC SCORING)



THE FIRST PREDICTIVE MODEL IN PROSTATE CANCER: DEVELOPED FOR THE RADIATION DECISION-MAKING PROCESS (PELVIS XRT: y/n)

The Roach Equation:
Risk of LNI = (GPS x 15) – 60

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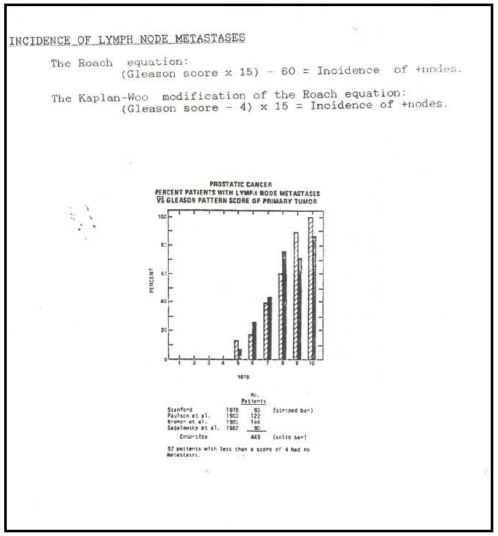
The Kaplan - Woo modification of the Roach Equation:
Risk of LNI = (GPS – 4) x 15

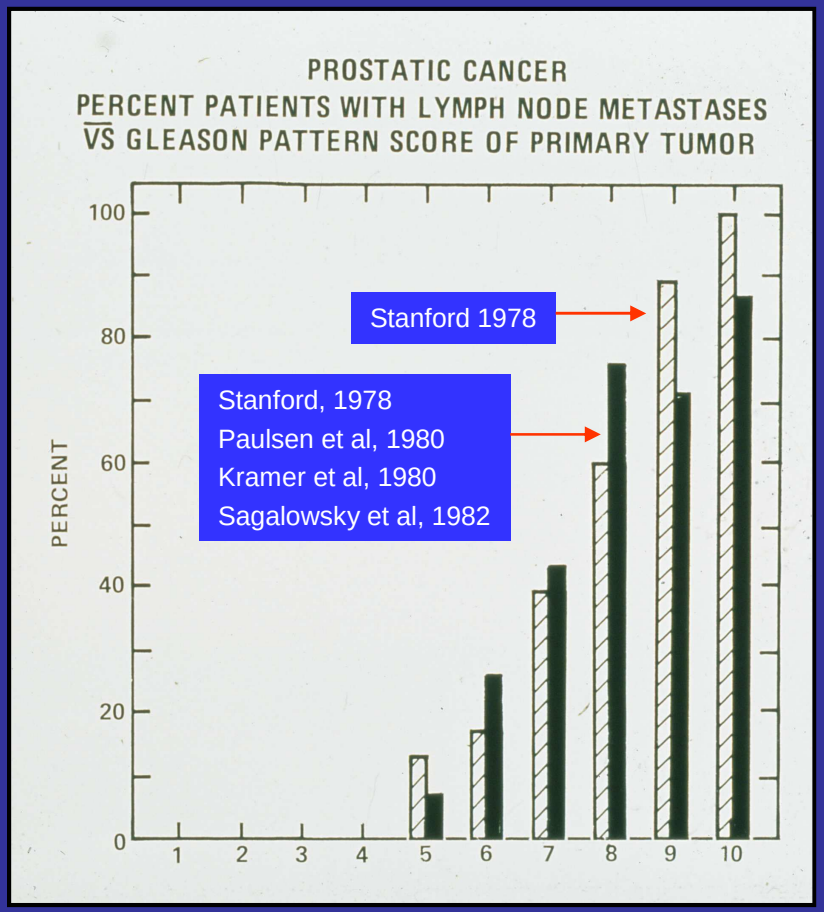
The Prostate Club, Stanford, May 1987



INCIDENCE OF LYMPH NODE METASTASES

The Roach equation:
(Gleason score x 15) - 60 = Incidence of +nodes.

The Kaplan-Woo modification of the Roach equation:
(Gleason score - 4) x 15 = Incidence of +nodes.



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