Natural History, GGO Treatment Algorithms and Concepts Going Forward

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No conflicts to disclose with respect to this presentation

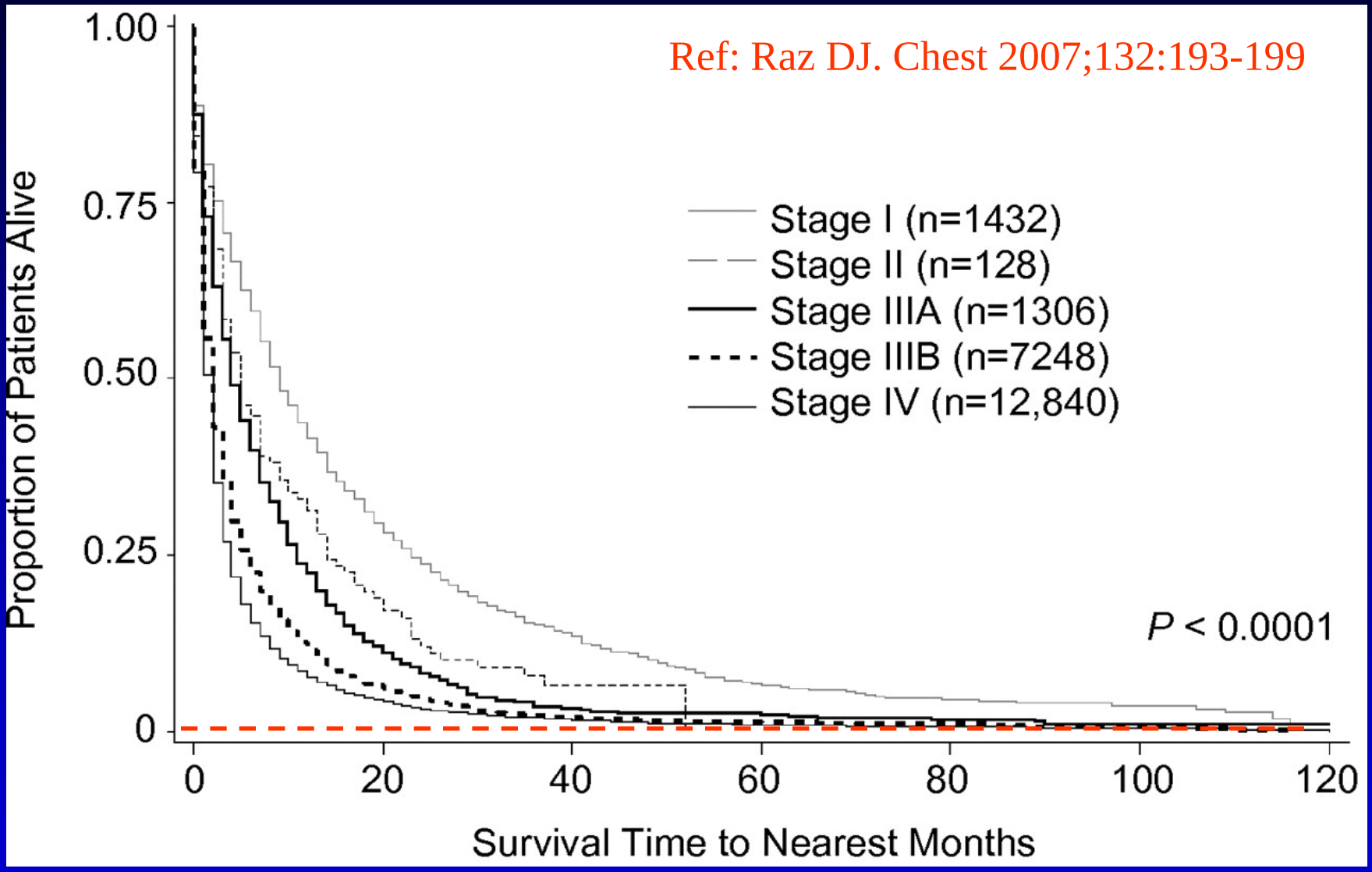
Natural History
Direct Measurement

Stage I,II: Natural History

Study	Yrs	N	How detected		MST (mo)	Overall Surv % 1-yr	2-yr	5-yr
Henschke	88-94	131	routine	cIa	(24)[a]	(81)[a]	(48)[a]	(39)[a]
Sobue	82-84	27	routine	cI	13	50	30	4
Raz	89-03	1,432	routine	cI	9	42	24	7
Wisnivesky	88-04	1,468	routine	cI	(14)[a]	(57)[a]	(32)[a]	(14)[a]
Chadha	90-01	26	routine	cI	10	39	0	0
McGarry	94-99	49	routine	cI	14	62	38	-
Motohiro	82-91	584	routine	cI	(17)[b]	(69)[b]	(36)[b]	(14)[b]
Vrdoljak	80-87	19	routine	cIb	17	80	20	0
Raz	89-03	128	routine	cII	5	33	13	3
Wisnivesky	88-04	140	routine	cII	(14)[a]	(37)[a]	(20)[a]	(10)[a]
Vrdoljak	80-87	31	routine	cIIb	11	40	8	0

[a] Disease Free Survival ; [b] various (ineffective) nonsurgical tmts used

Natural History: Direct Measurement



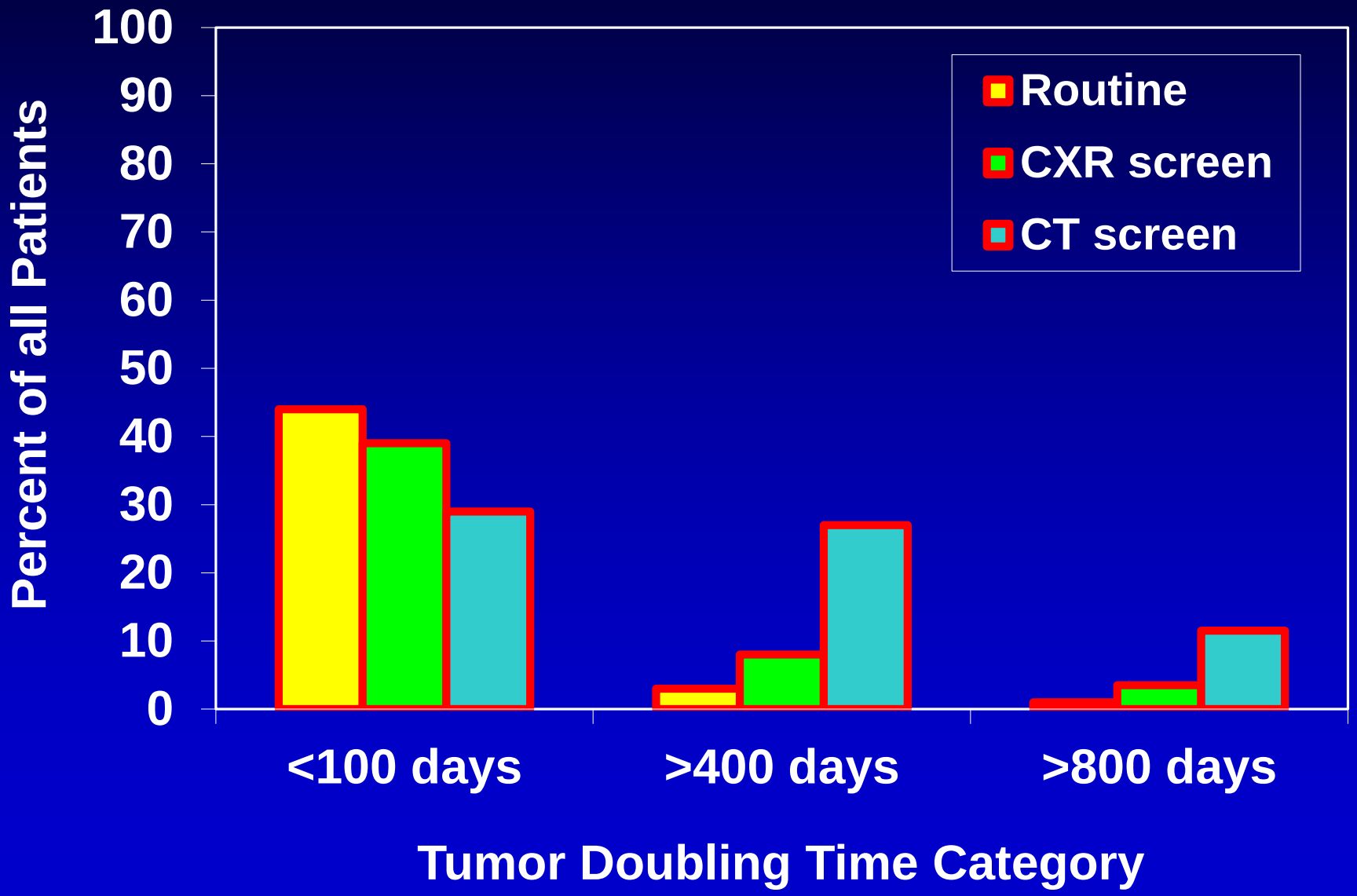
California Cancer Registry 1989-03; untreated patients

Tumor Doubling Time

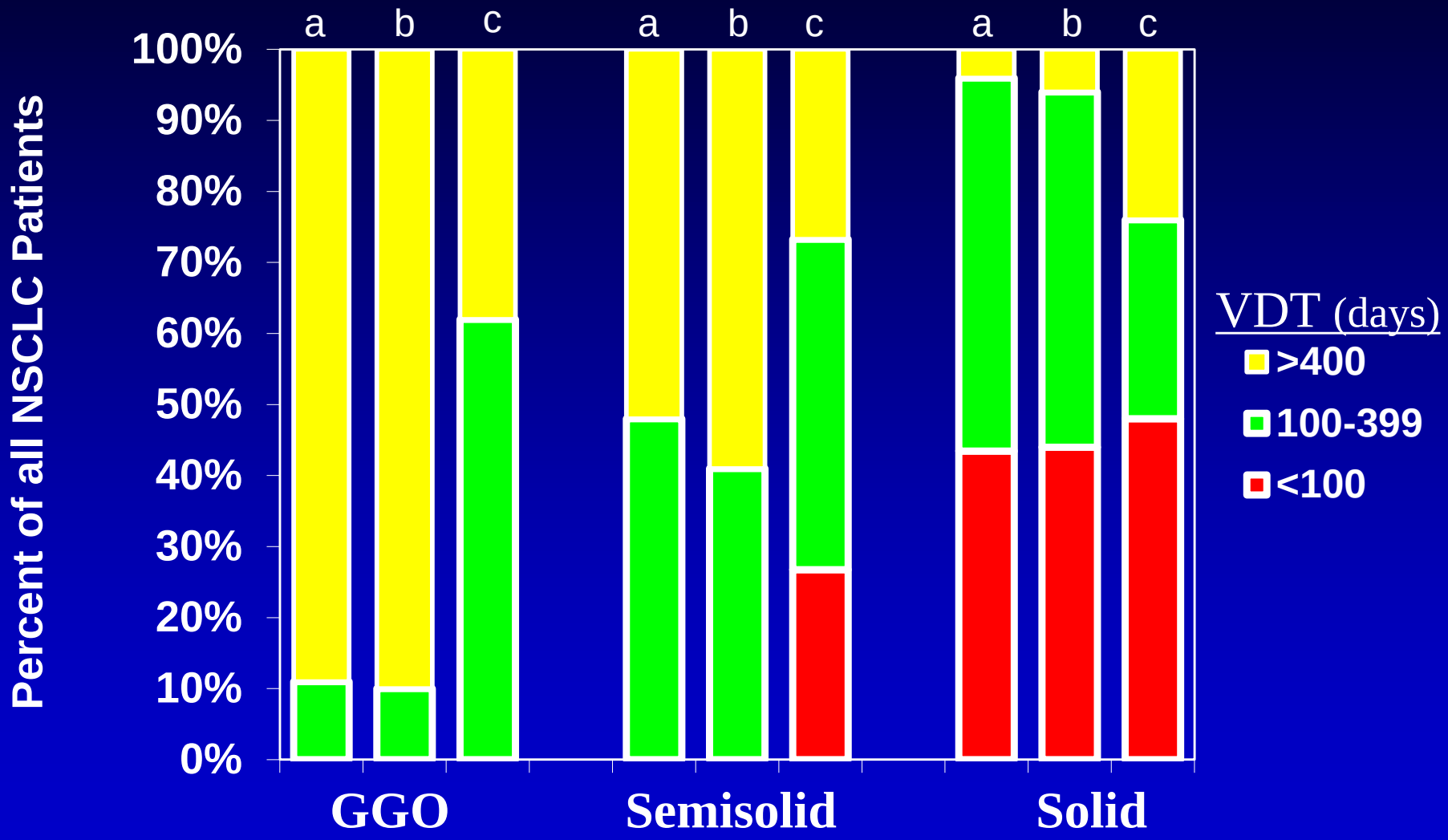
Tumor Doubling Time Distribution

Study	N	How detected	VDT (days) <100	100-249	250-399	>400
Garland	40	routine	48	38	8	6
Weiss	91	routine	48	40	7	4
Steele	67	routine	33	52	10	5
Kerr	23	routine	61	26	13	0
Average		**routine**	**44**	**42**	**10**	**3**
Arai	237	CXR screen	37	29	22	14
Usuda	159	CXR screen	47	37	6	10
Yankelowitz	44	CXR screen	48	4	5	2
Yankelowitz	43	CXR screen	23	52	18	7
Average		**CXR screen**	**39**	**42**	**12**	**8**
Hasegawa	61	CT screen	24	31	19	26
Sone	45	CT screen	18	20	18	45
Lindell	48	CT screen	33	23	17	27
Average		**CT screen**	**29**	**27**	**18**	**27**

Distribution of Volume Doubling Times of NSCLC by Method of Detection



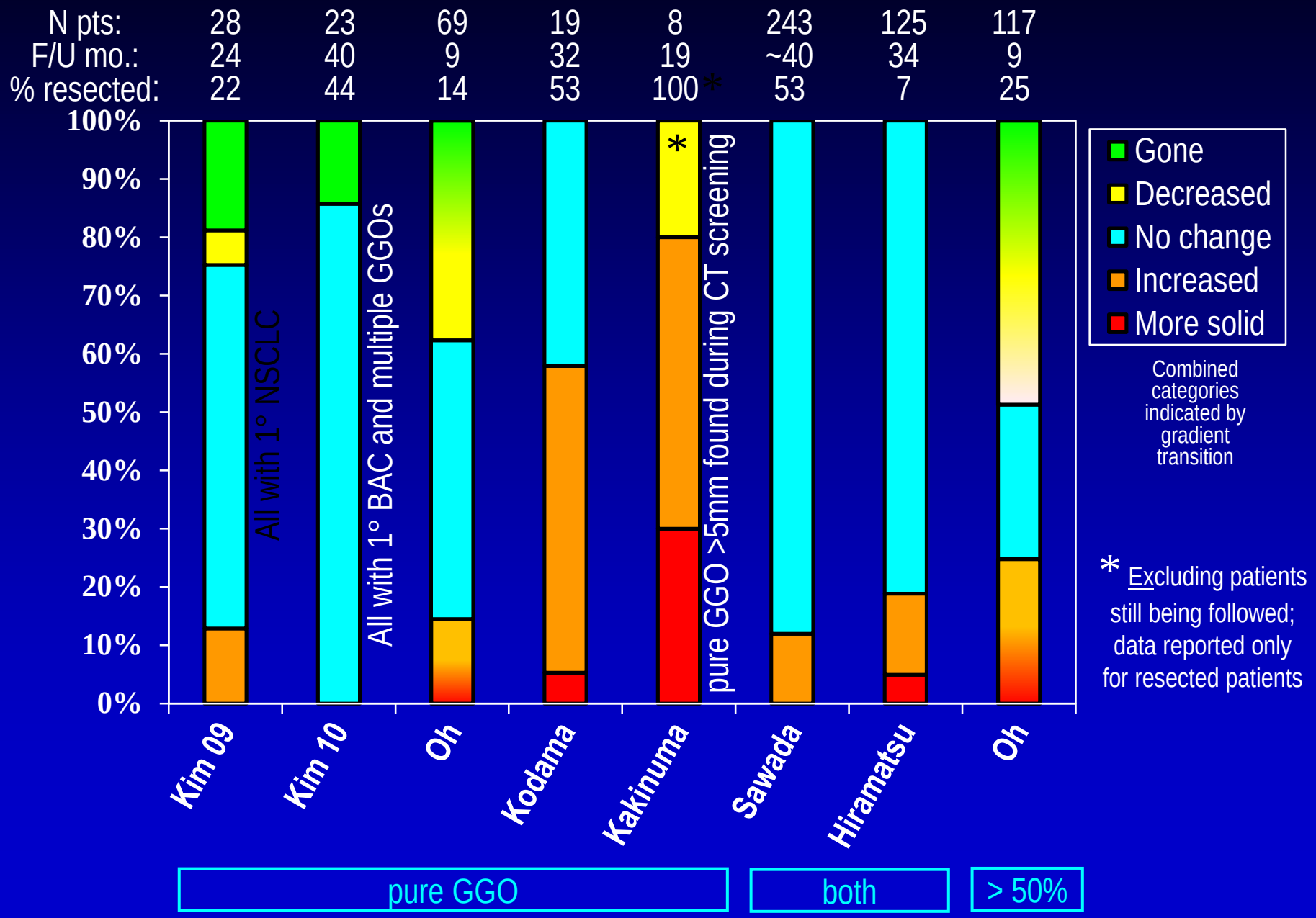
Distribution of Doubling Times of NSCLC detected by CT-Screening by Radiographic Type



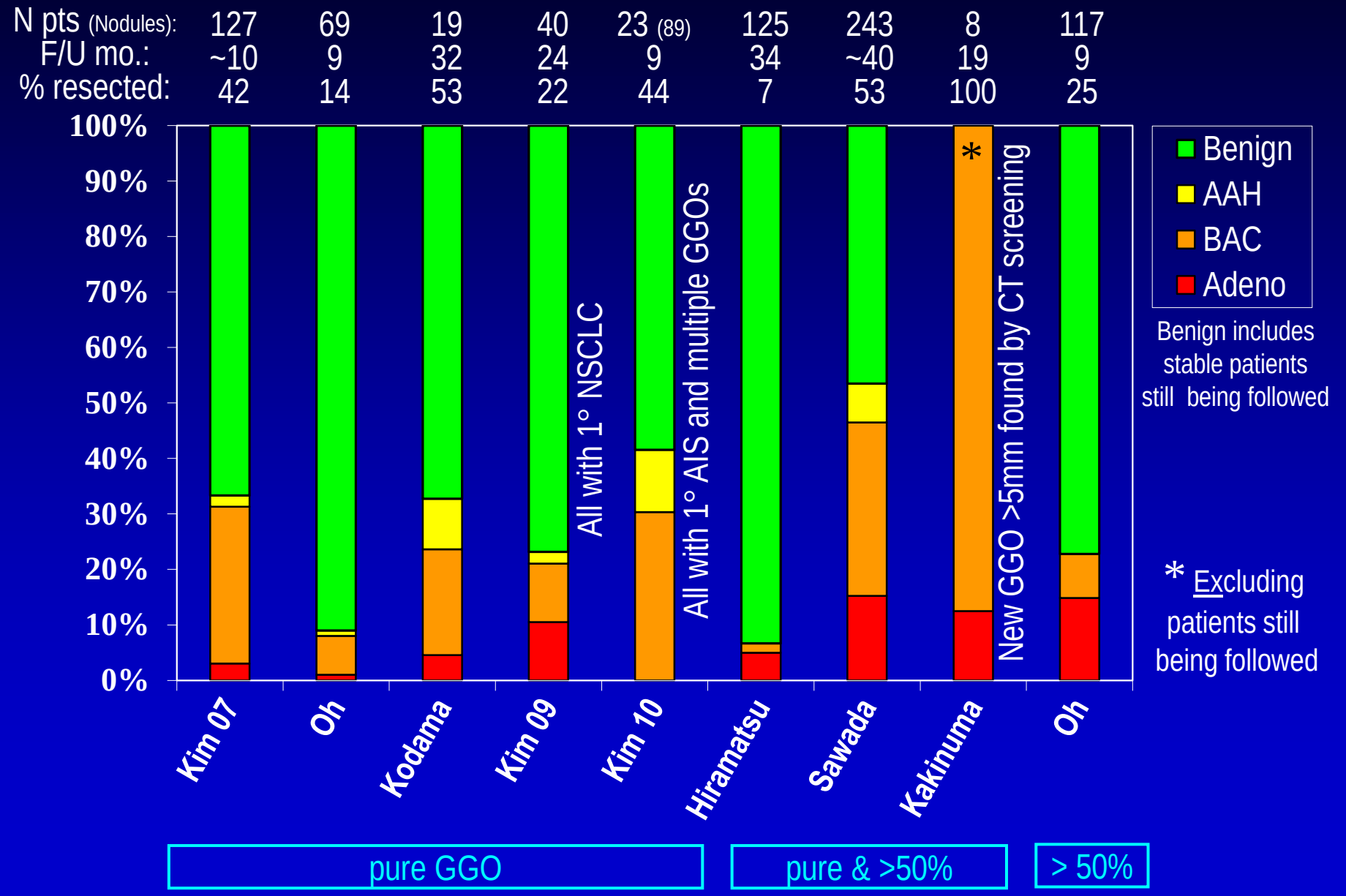
a: Hasegawa. Br J Radiol 2000;73:1252-59. b Sone S. Lung Cancer 2007;58:329-41
c: Lindell. Radiology 2007;242:555-62

Natural History of GGO

Outcomes during Observation



Diagnoses made during Observation

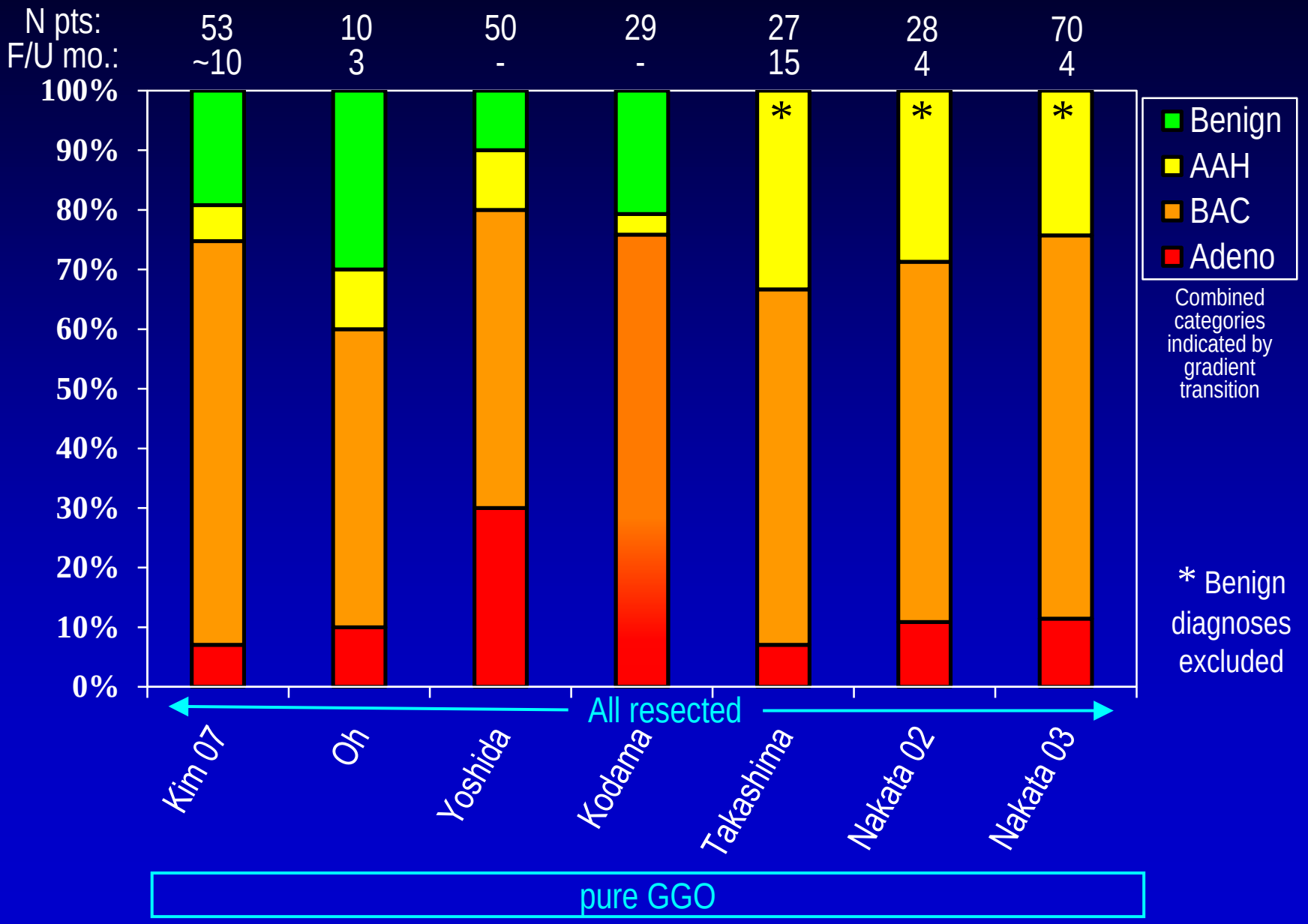


Natural History of GGO

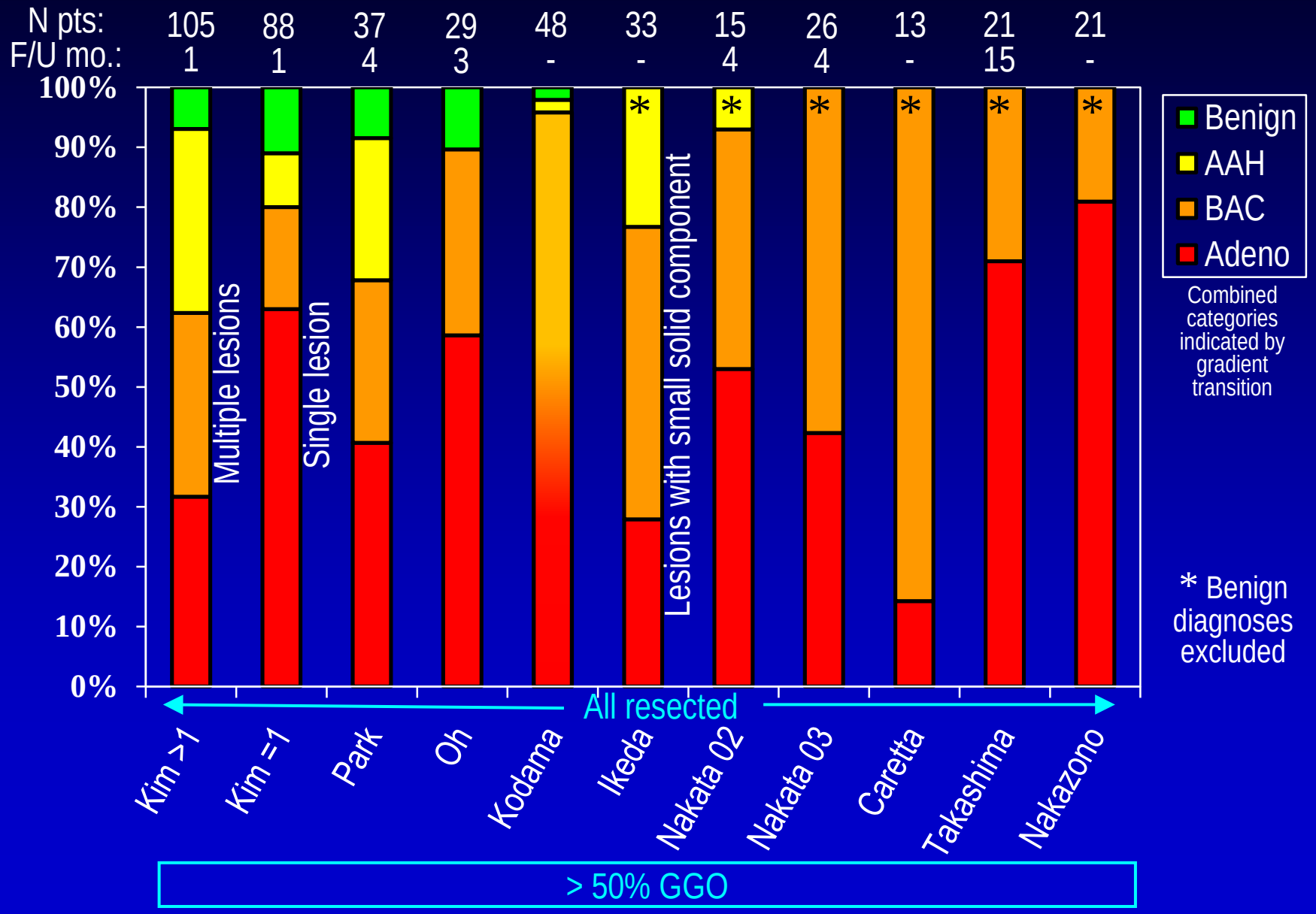
- ~20% disappear
  Vast majority during first 3 mo
- ~10% ↓ in ∅
  But among adenoCa with an initial period of observation, ~20% ↓ in ∅ (some with development of solid component)
- ~50% no change
- ~20% of pure GGO will ↑ in ∅
  Duration of f/u of 1-3 yrs in most studies
- Eventually ~5% found to be Adeno, ~20% BAC
  ~2x higher rate for semisolid GGO

Triggers for Intervention

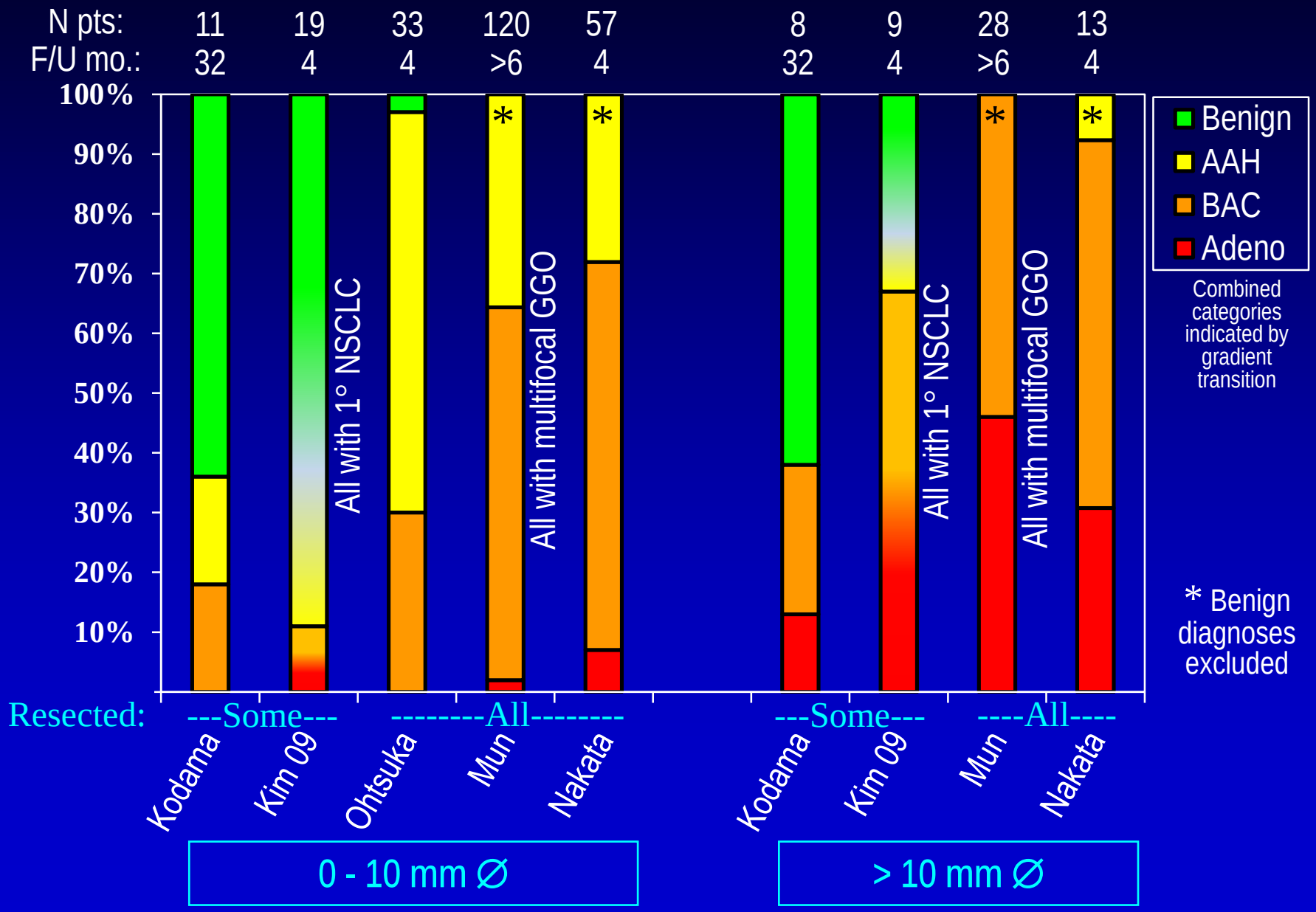
Findings at Resection of a pure GGO



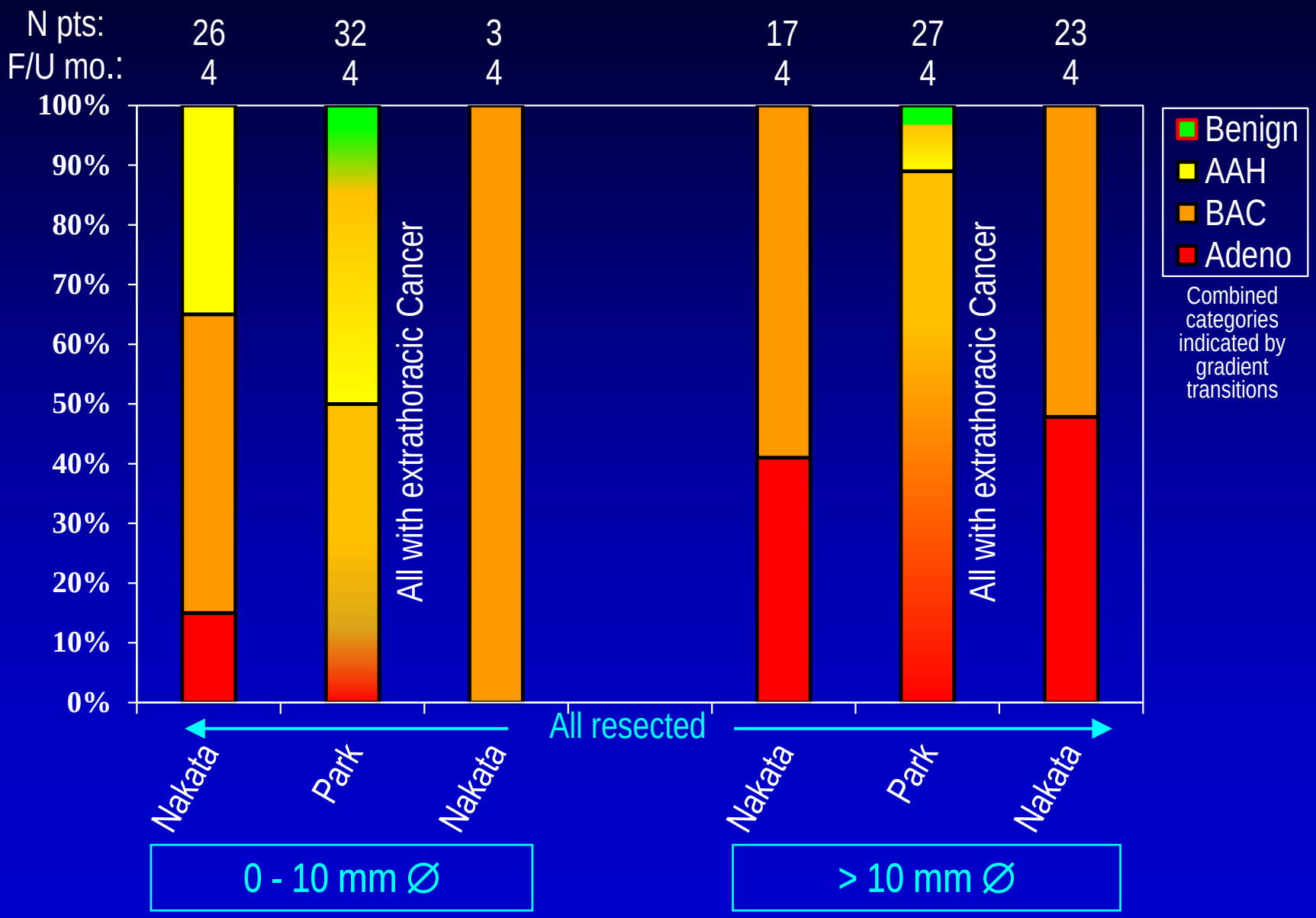
Findings at Resection of >50% GGO



Effect of Size for Pure GGO



Effect of Size for Semisolid GGO



Pure Ground Glass Opacities

≤ 10mm: CT in 1 yr

- *Rationale*: with observation invasive Ca in <10% over ~3 yrs is (all sizes)
- at resection most are benign, 0-5% Adeno, +20% BAC/AIS/MIA

> 10-15 mm: CT in 3-6 months, if still present resect

- *Rationale:* with observation invasive Ca in <10% over ~3 yrs is (all sizes)
- at resection moderate chance of inv Ca ~10-20%, +20-40% BAC/AIS/MIA

>15mm: CT in 3 months, if still present resect

- *Rationale:* Can't quantify risk but likely even higher

Algorithm for F/U of Nodules

Previous pure GGO, now with a new solid component or **clear increase in density, or ≥ 25% ↑ ∅ in 1 yr (= VDT ≤1 yr)**

< 5mm:

Repeat CT in 3 months, if no change then resect; but if clinically very suspicious, resect

Rationale: chance of inv cancer unclear, but probably >20%

5- 10mm: Resect

Rationale: chance of inv cancer unclear, but probably ~50%

> 10 mm: Resect

Rationale: chance of inv cancer unclear, but probably >>50%

Pure GGO, < 25% ↑ ∅ in 1 yr (= VDT >1 yr)

<10 mm:

Repeat CT in 6 months, if continued †, resect; if no change then CT in 6 months

Rationale: chance of inv cancer unclear, but probably ~10%

10-15 mm:

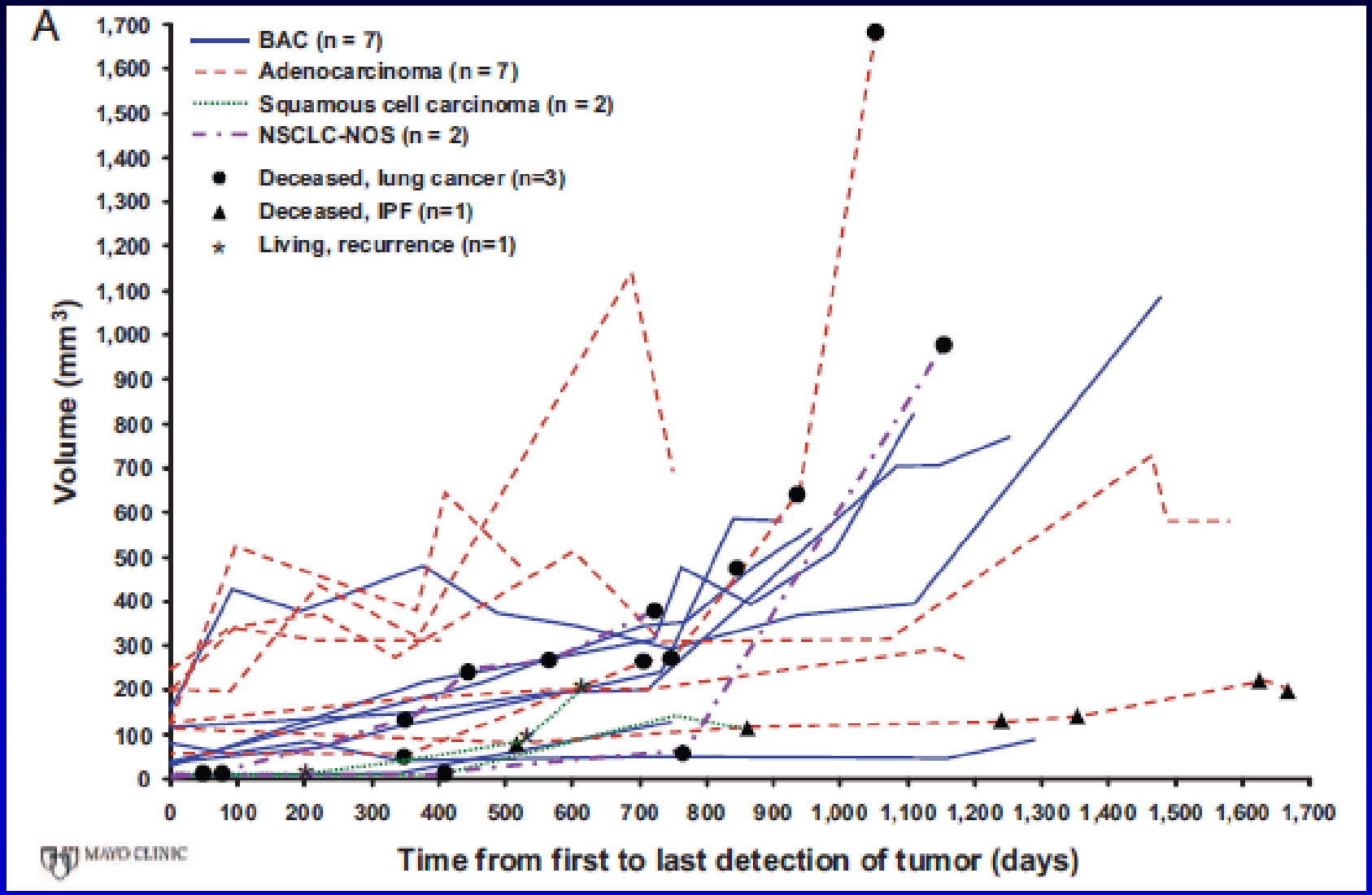
Repeat CT in 3 months, if continued † or if no change, resect; if ↓ then CT in 6 months

Rationale: chance of inv cancer unclear, but probably 10-20%

> 15 mm:

Resect (hard to imagine this scenario, because we would resect anyhow if >115mm on BL scan

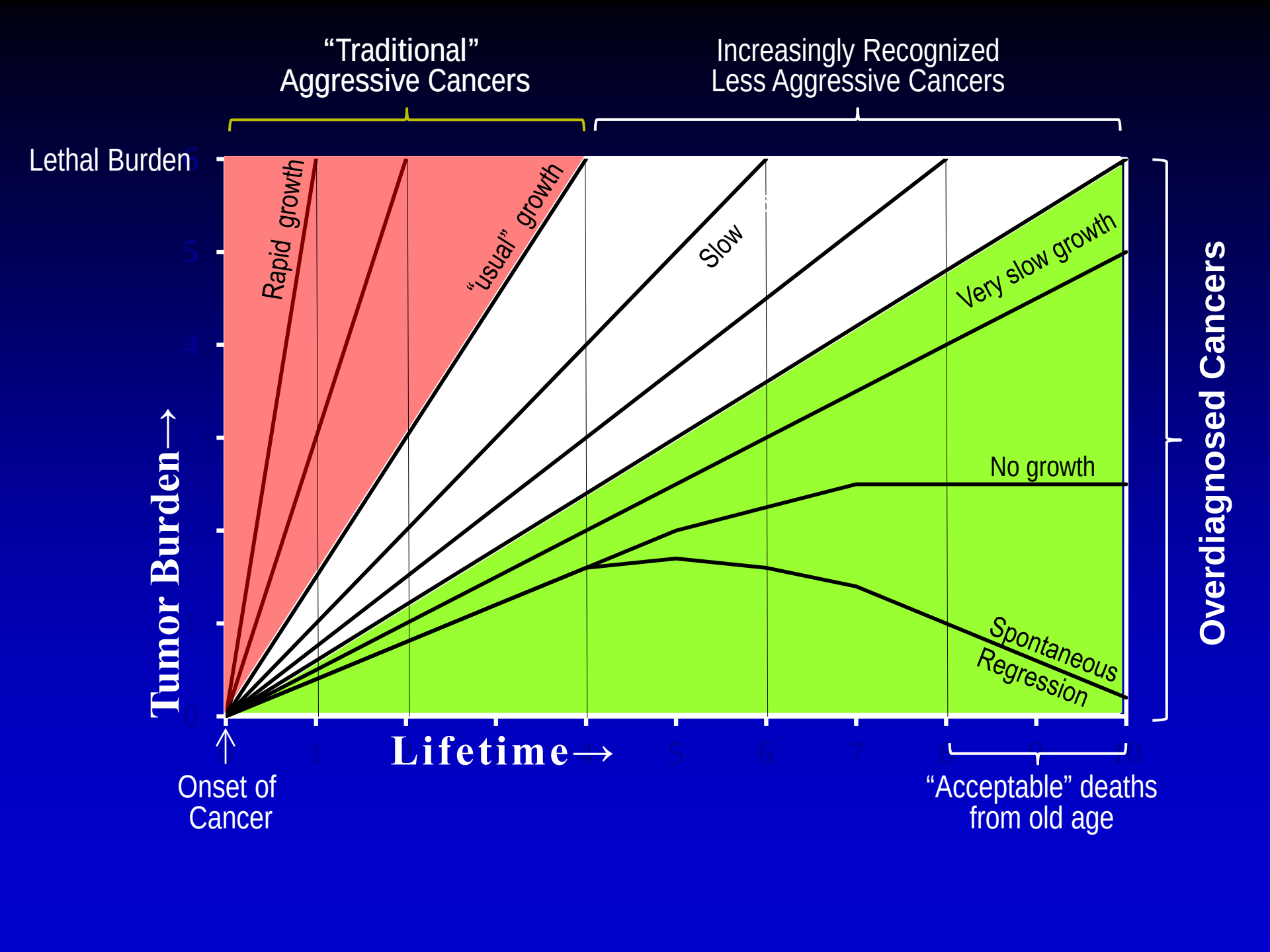
Rate of Growth over Time: CT screening data

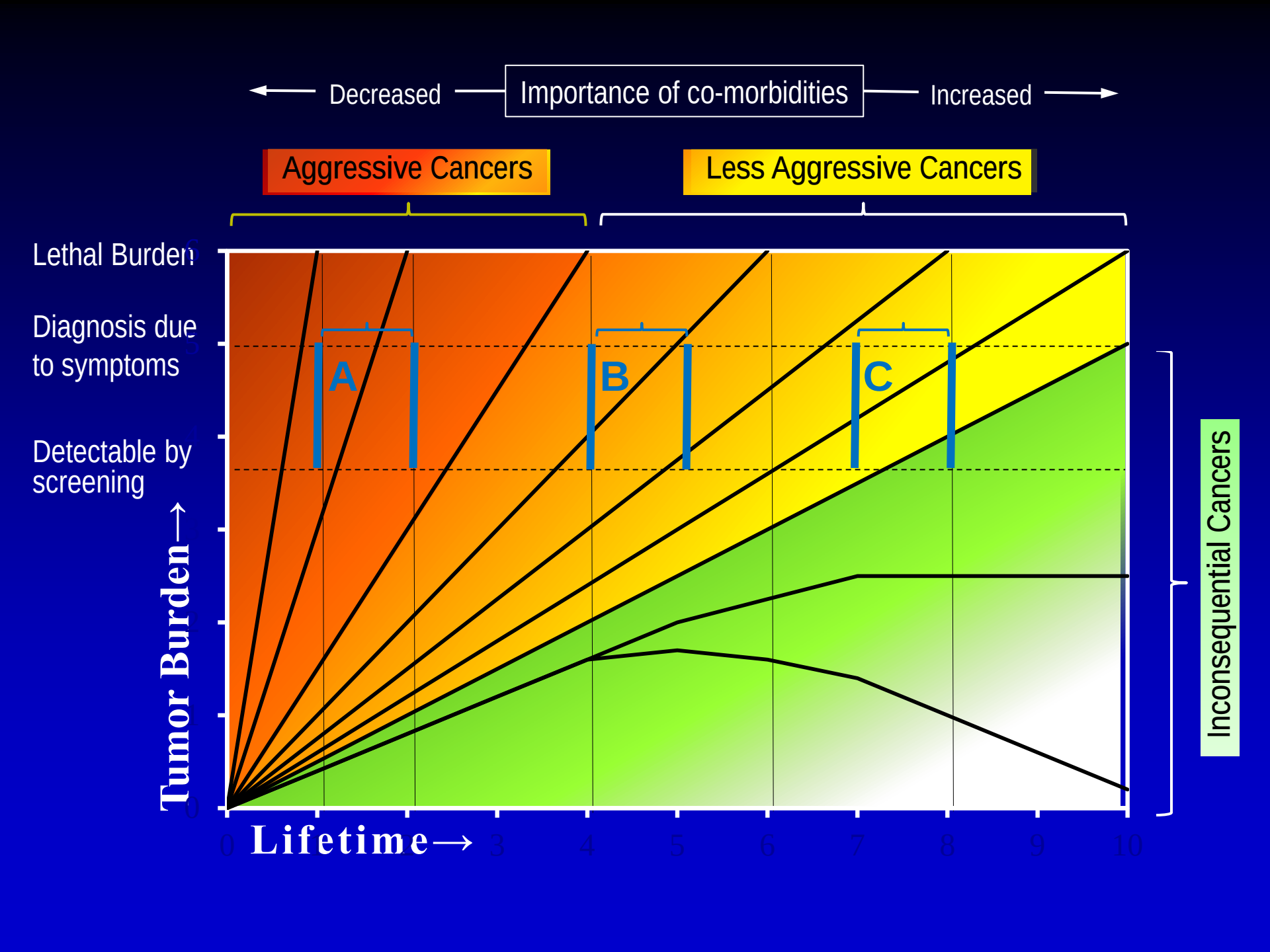


Ref: Lindell Chest 2009;136:1586

Problems with Predicting Behavior

- Does growth rate predict when metastasis will occur?
- How reliably can we measure size / growth?
- Is the growth rate constant over long periods of time?
- How do we gain knowledge without doing a long term natural history study?
- How do we develop tools to learn from observations gained from systems of care, rapidly changing conditions


"Traditional"
Aggressive Cancers
Increasingly Recognized
Less Aggressive Cancers
Lethal Burden
Rapid growth
"usual" growth
Slow
Very slow growth
No growth
Spontaneous
Regression
Overdiagnosed Cancers
Tumor Burden→
Lifetime→
Onset of
Cancer
"Acceptable" deaths
from old age


Decreased
Importance of co-morbidities
Increased
Aggressive Cancers
Less Aggressive Cancers
Lethal Burden
Diagnosis due to symptoms
Detectable by screening
A
B
C
Inconsequential Cancers
Tumor Burden→
Lifetime→
0
3
4
5
6
7
8
9
10