

Case #2
T3 Breast Cancer in a
Postmenopausal Patient

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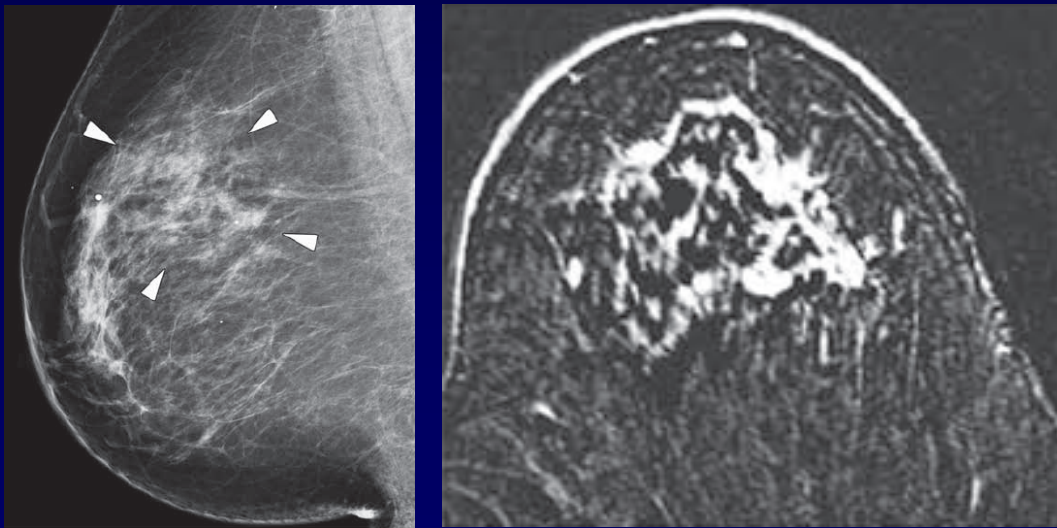
Clinical Case

- † 59-years-old, palpable thickening in the upper right breast
- Grade I-II invasive lobular carcinoma (ILC)
ER+85%, PR+70%, HER2-
- LVEF 65%, hypertension, ACE inhibitor,
ECOG PS 0

cT3N0M0

Question 1: MRI Before Neoadjuvant Therapy (NAT)?

- ILC (8% to 14%)
 - More often multicentric, bilateral
 - Sensitivity mammography 57% to 81%
 - Spiculated or ill-defined margins

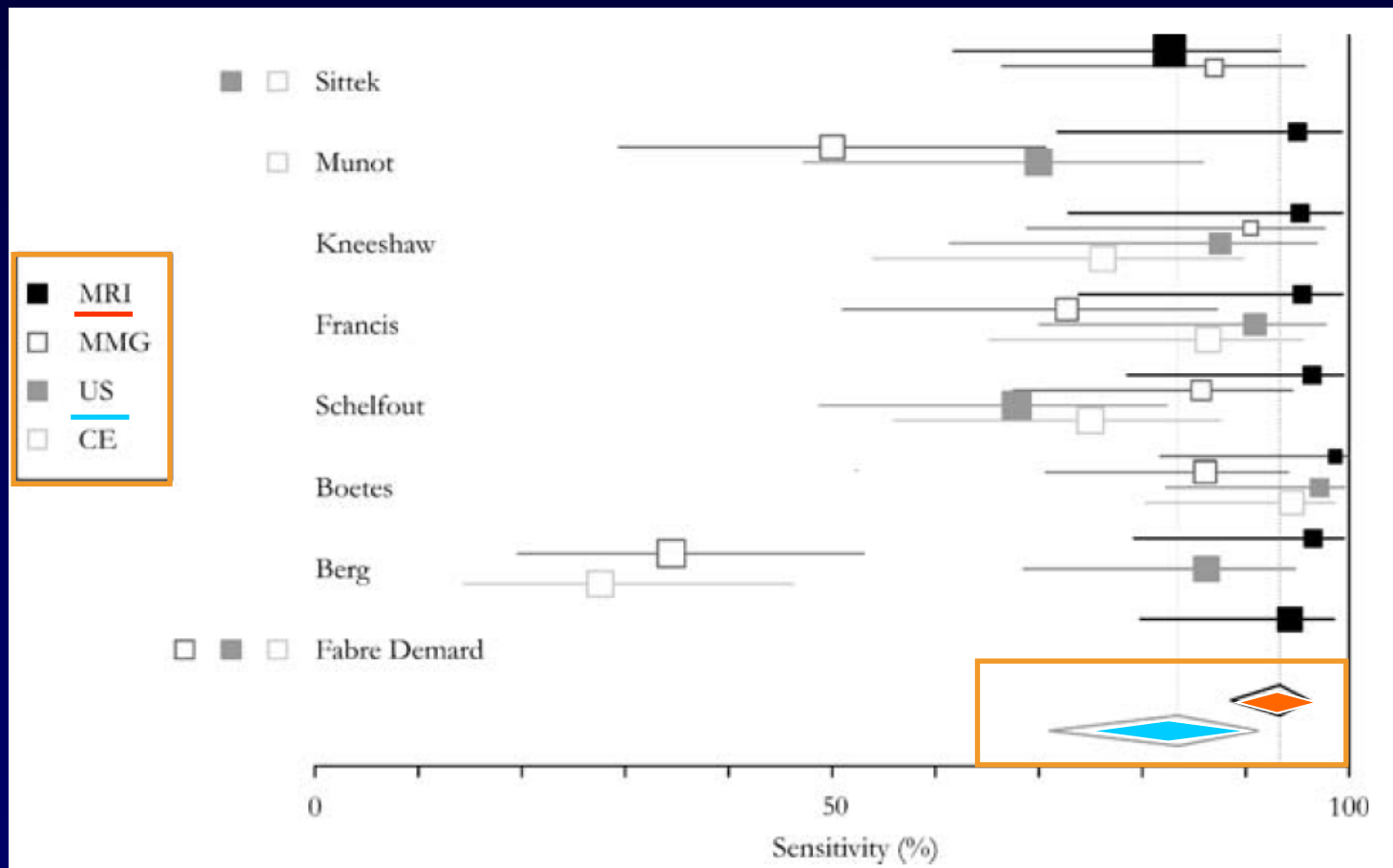


MRI compared to conventional diagnostic work-up in the detection and evaluation of invasive lobular carcinoma of the breast: a review of existing literature

Ritse M. Mann · Yvonne L. Hoogeveen ·
Johan G. Blickman · Carla Boetes

Breast Cancer Res Treat (2008) 107:1–14

Mammography data too heterogeneous for pooled estimate

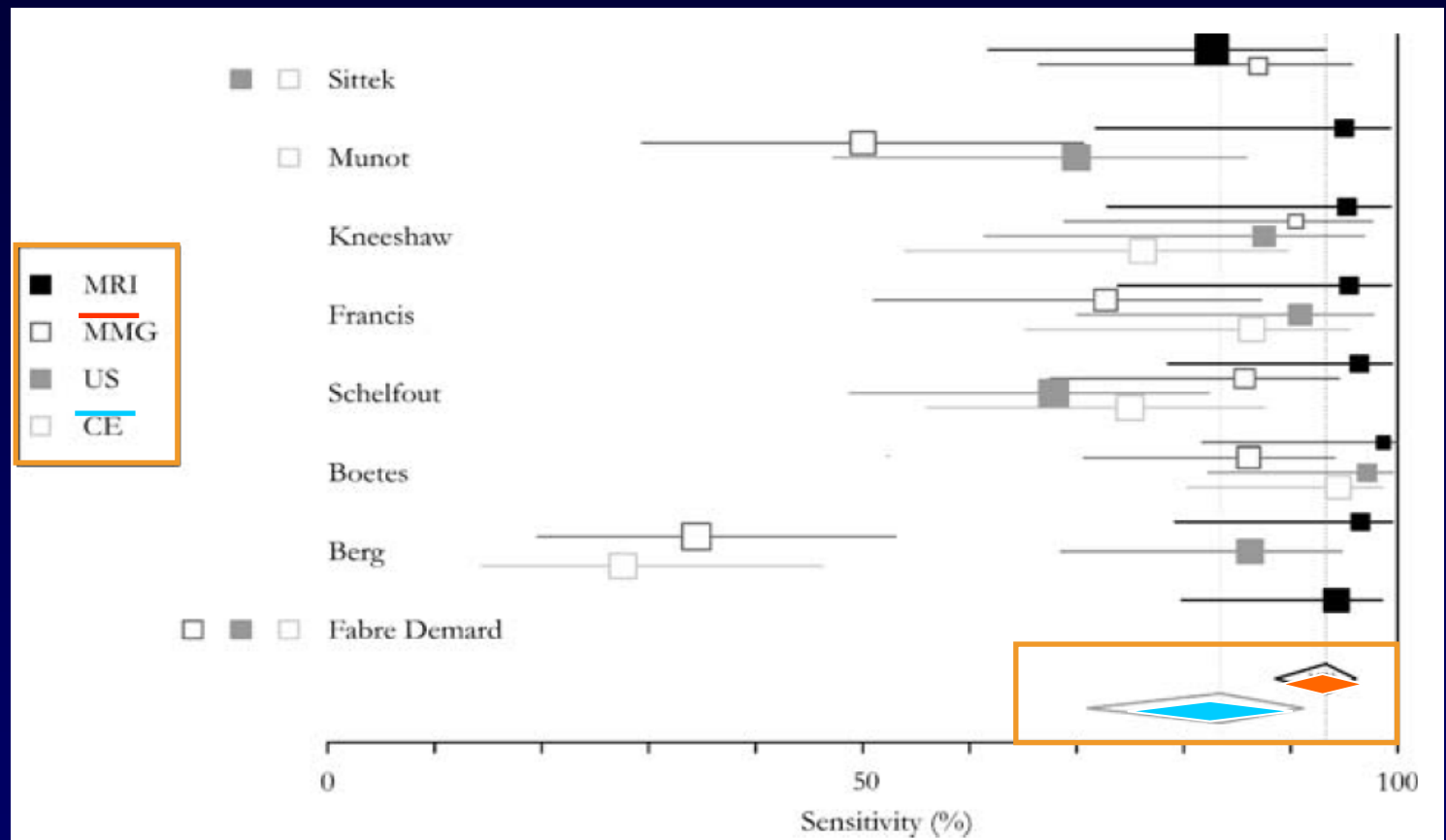


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Mammography data too heterogeneous for pooled estimate



MRI provides additional knowledge that cannot be obtained by conventional imaging modalities

Question 1: MRI Before NAT?

Evaluation of tumor size and spread

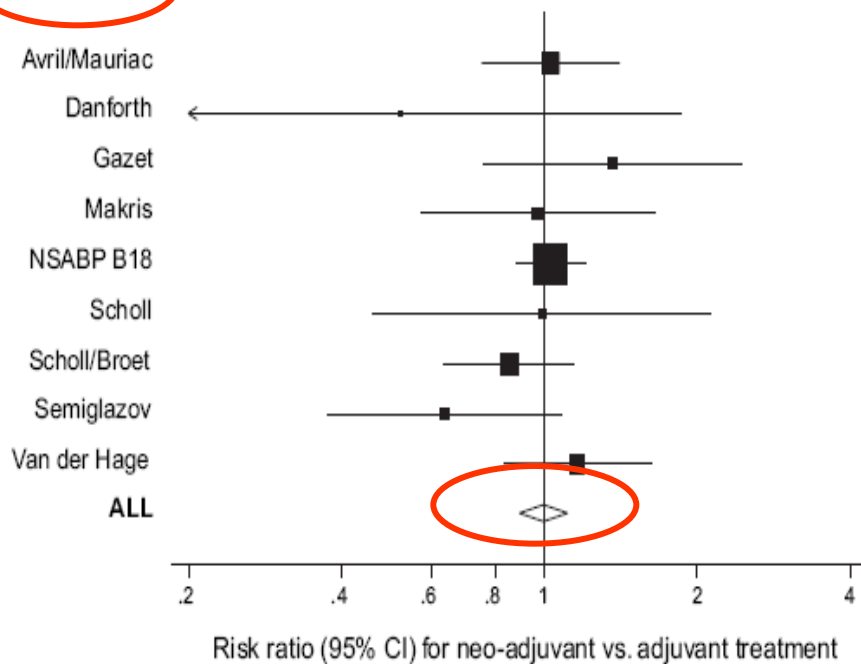
Baseline measurement response to NAT

NAT Versus AT

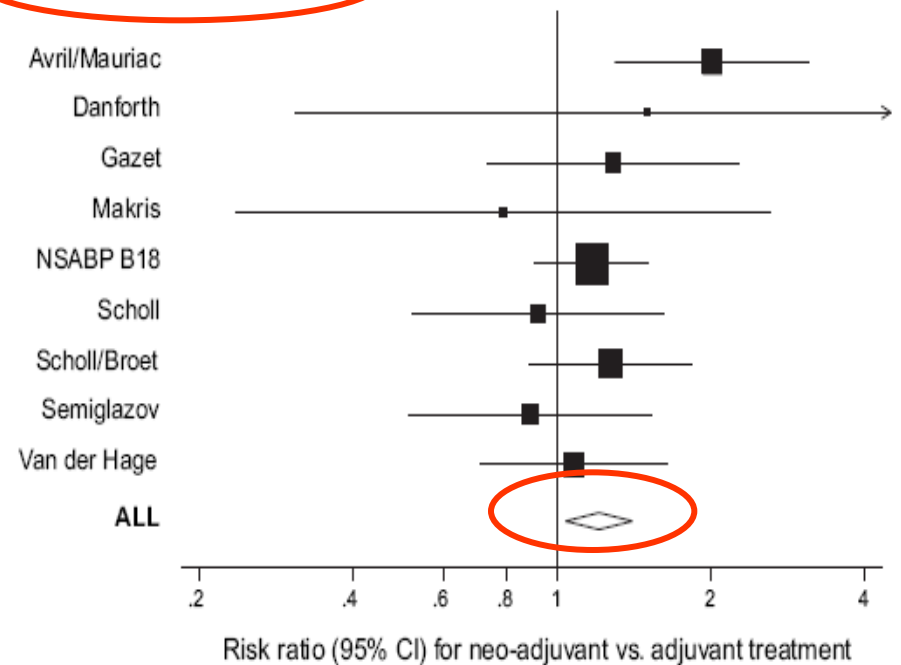
Neoadjuvant Versus Adjuvant Systemic Treatment in Breast Cancer: A Meta-Analysis

Daive Mauri, Nicholas Pavlidis, John P. A. Ioannidis

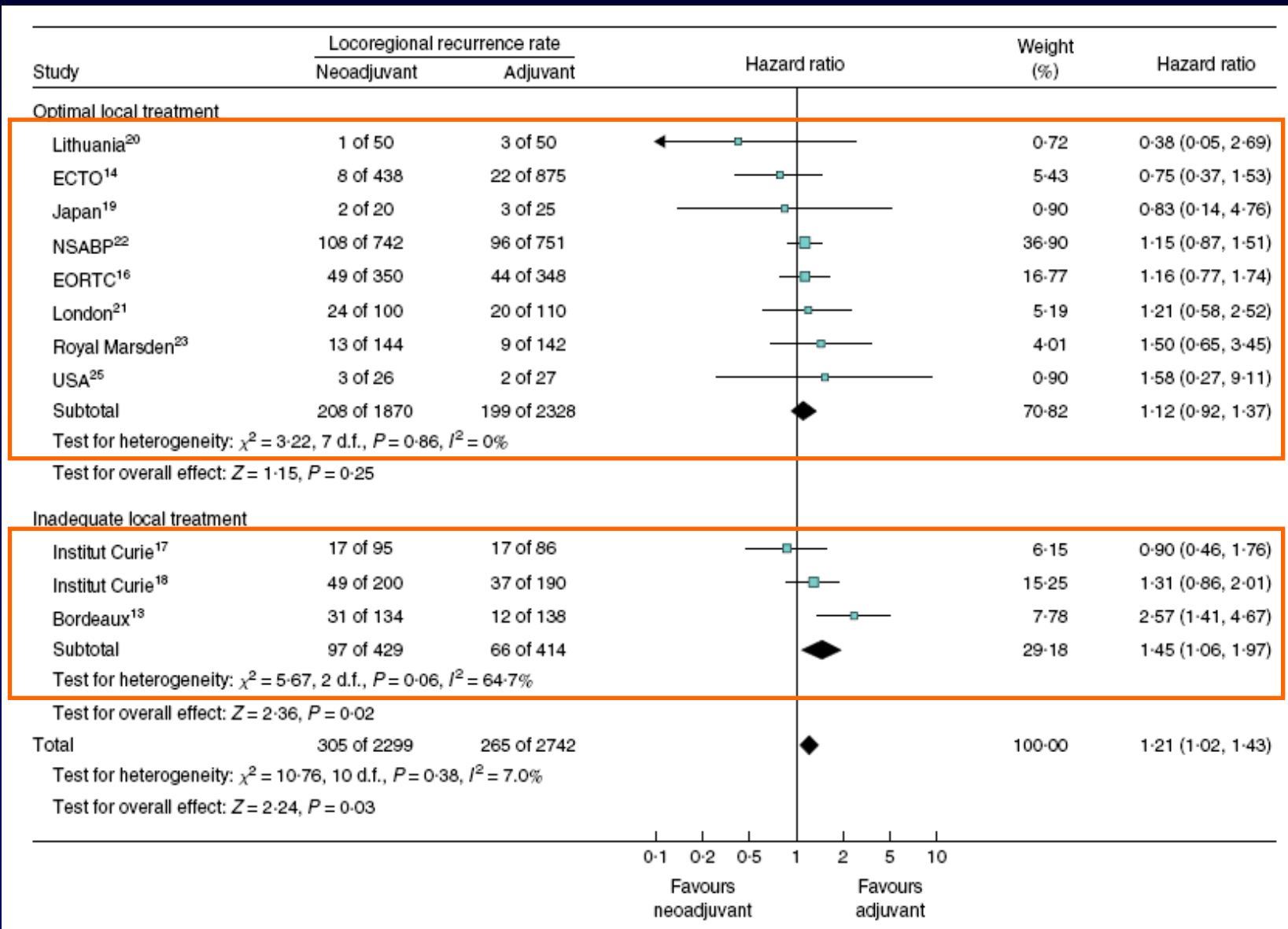
A Death



D Loco-regional recurrence



AT Versus NAT: Optimal Local Treatment



Radiotherapy only

Advantages NAT

Downsizing of the tumor

- Inoperable → Operable
- Mastectomy → Breast-conserving surgery
- Breast-conserving surgery → Better cosmesis
- Avoidance of axillary lymph node dissection (downstaging)

In situ monitoring of the efficacy of systemic therapy

- Switching of systemic treatment
- Assessment of surrogate biological endpoints
- Advancement of new drug development

Question 1: Which NAT?

pCR to Neoadjuvant Chemotherapy in ER+ Patients

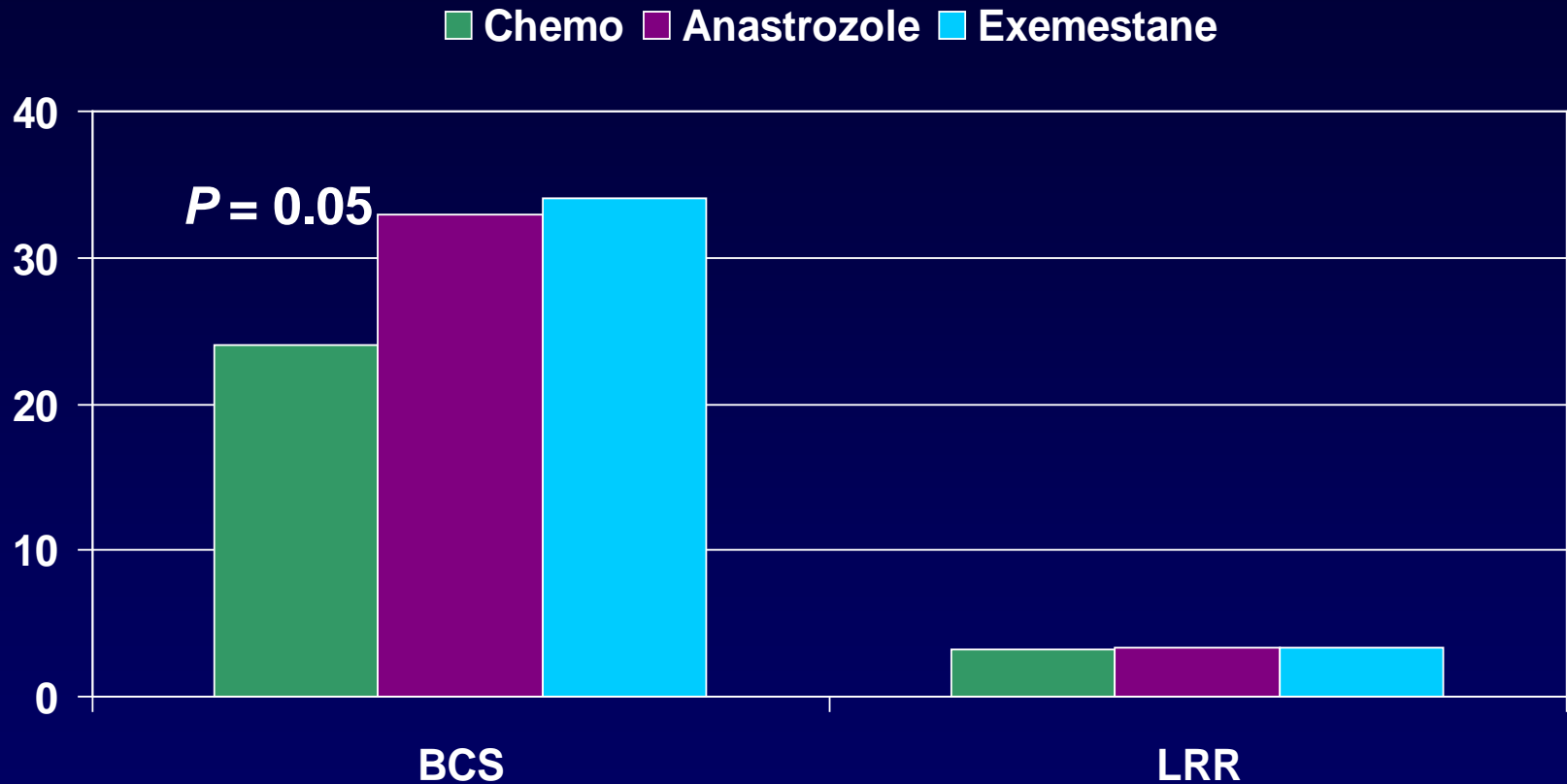
Author	No. of Patients	Regimen	% HR Negative	% pCR in HR Negative	% pCR in HR Positive
Houston (pooled data)	1,018	Pooled data	NA	20.6	5.6
von Minckwitz et al ⁴ (Geparduo)	913	dd AD/AC- docetaxel	26.3	22.8	6.2
Gianni et al ⁵⁰ (ECTO)	438	AP-CMF	38.2	42.2	11.6
Bear et al ²¹ (NSABP-B27)	2411	AC v AC-docetaxel	32	16.7	8.3
von Minckwitz et al ⁵ (Gepartrio)	286	DAC/DAC-NX	31.9	36.6	10.1
von Minckwitz et al ³⁰ (Gepardo)	250	dd AD+/Tam	43.9	15.4	1.1

Abbreviations: dd, dose dense; pCR, pathologic complete remission; HR, hormone receptor; NA, not available; AD, doxorubicin and docetaxel; AC, doxorubicin and cyclophosphamide; ECTO, European Cooperative Trial in Operable Breast Cancer; AP, doxorubicin and paclitaxel; CMF, cyclophosphamide, methotrexate, and fluorouracil; DAC, docetaxel, doxorubicin and cyclophosphamide; NX, vinorelbine and capecitabine; Tam, tamoxifen.

ER+ predictive for low % pCR in neoadjuvant chemotherapy

Question 1: Which NAT?

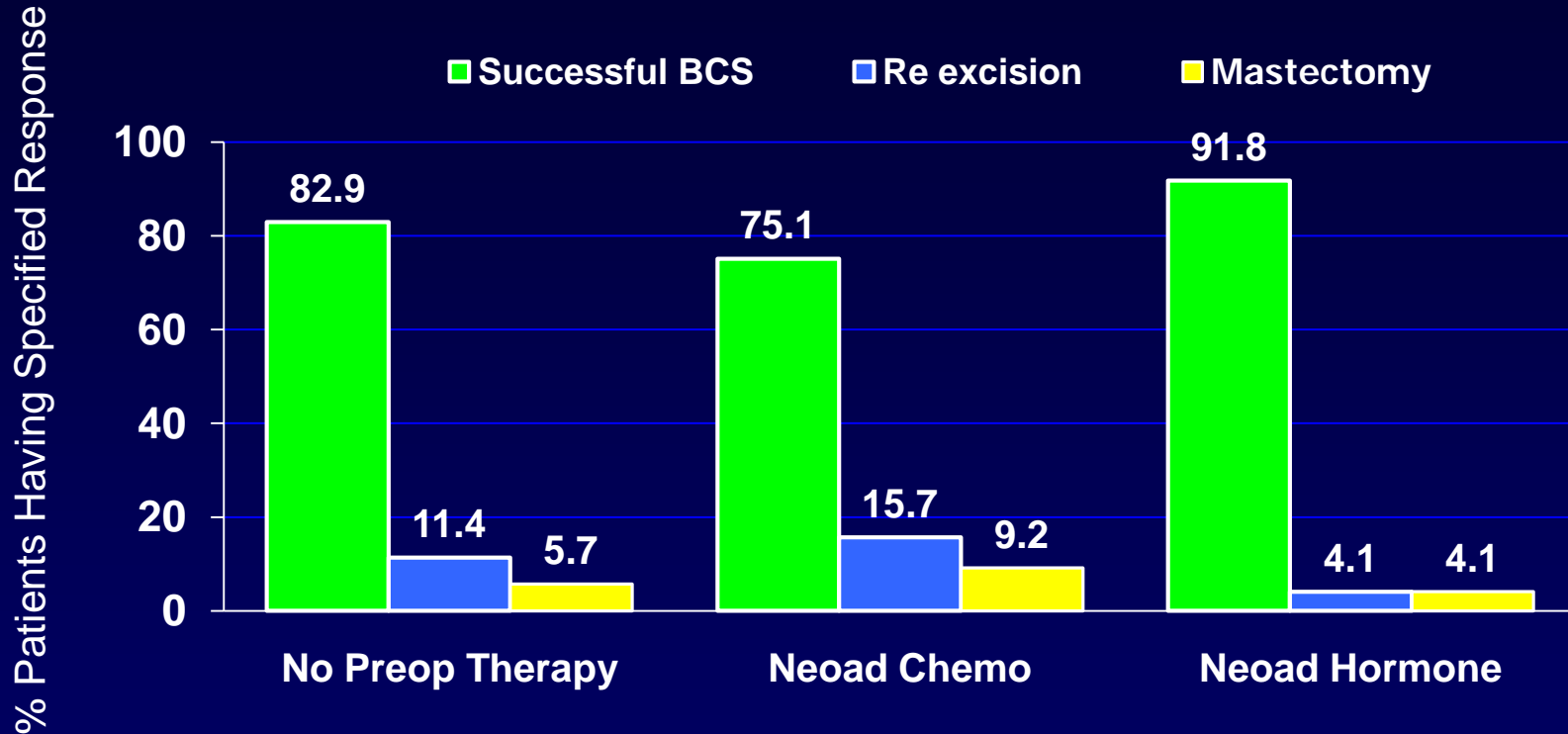
Hormone Therapy Versus Chemotherapy



Neoadjuvant hormone therapy at least as effective in downsizing as chemotherapy in ER+ patients

Question 1: Which NAT?

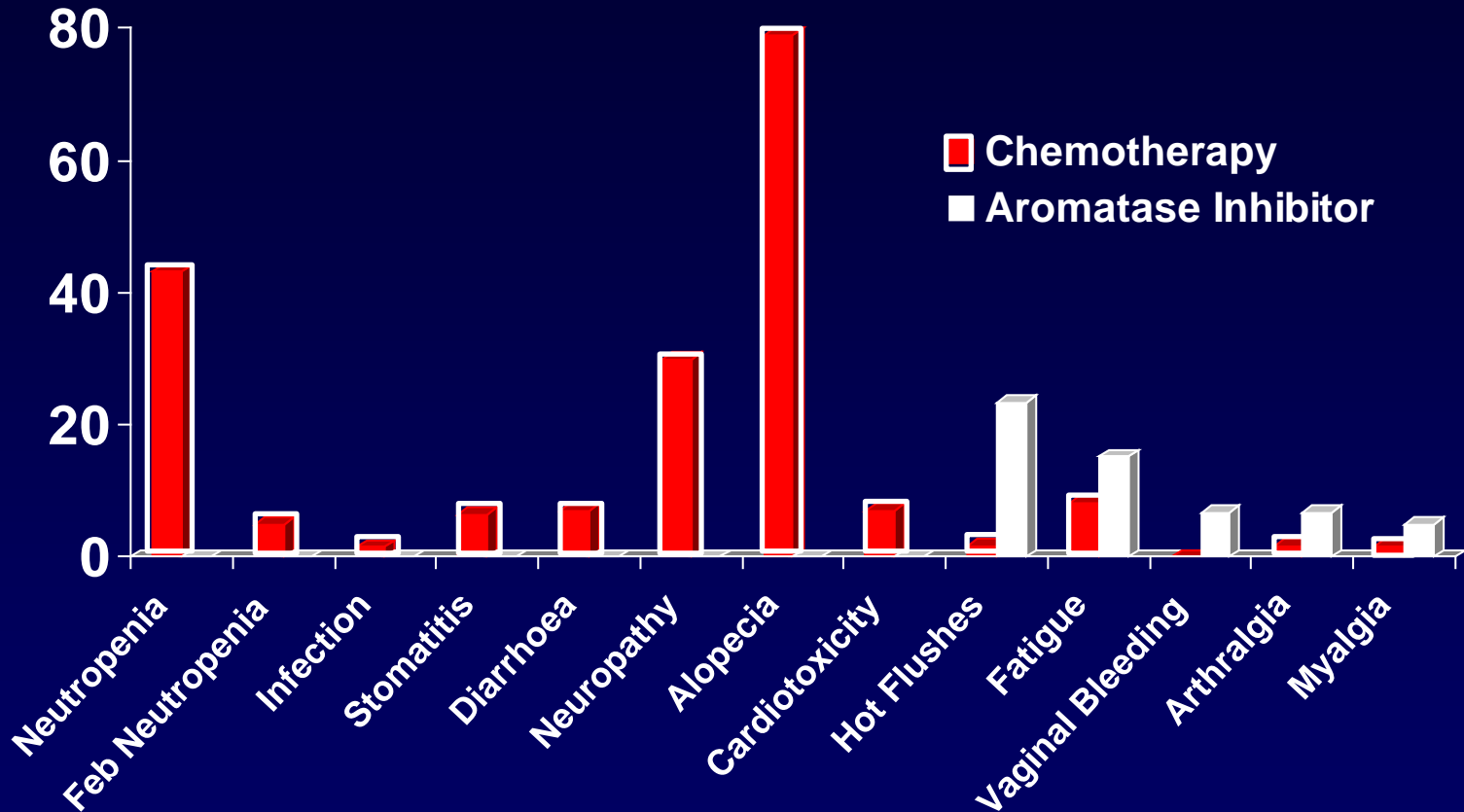
Hormone Therapy Versus Chemotherapy



ER patients probably benefit more from neoadjuvant HT compared to neoadjuvant CT

Question 2: Which NAT?

Side Effects AI Versus CT



AI favorable side effects compared to chemotherapy
Especially feasible in elderly women / comorbidity

Question 2: Which NAT?

Aromatase Inhibitors (AIs) versus Tamoxifen

	Drug	N	Clinical Response	US Response	Increase BCS	
P024¹ <i>4 months</i>	Letrozole	154	55%	35%	45%	<i>P</i> = 0.022
	Tamoxifen	170	36%	25%	35%	
IMPACT² <i>3 months</i>	Anastrozole	113	37%	24%	46%	<i>P</i> = 0.03
	Tamoxifen	108	36%	20%	22%	
	Both	109	39%	28%	26%	
PROACT³ <i>3 months</i>	Anastrozole	228	50%	40%	38%	<i>ns</i>
	Tamoxifen	223	46%	35%	30%	

1. Ellis M, et al. *Breast Cancer Res Treat.* 2007;105(Suppl 1):33-43. 2. Smith IE, et al. *J Clin Oncol.* 2005;23(22):5108-5116. 3. Cataliotti L, et al. *Cancer.* 2006;106(10):2095-2103.

Question 2: Which NAT?

Aromatase Inhibitors (AIs) versus Tamoxifen

	Drug	N	Clinical Response	US Response	Increase BCS	
P024 ¹	Letrozole	154	55%	35%	45%	$P = 0.022$
<p>Neoadjuvant HT effective in downsizing tumor</p> <p>AI seems to be more effective than tamoxifen</p>						
	Both	109	39%	28%	26%	
PROACT ³	Anastrozole	228	50%	40%	38%	ns
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Question 3: Timing SLNB

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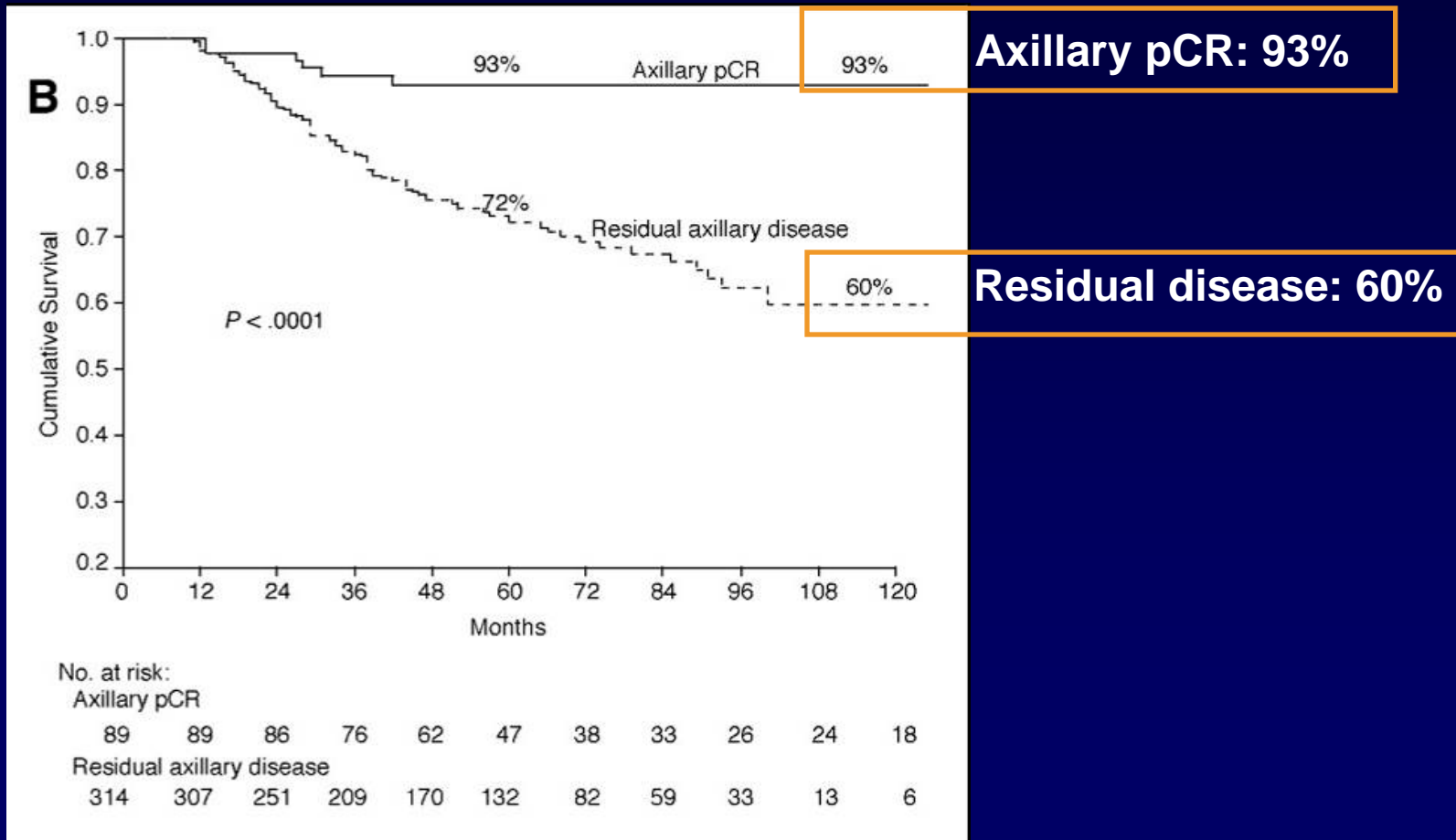
In situ monitoring of the efficacy of systemic treatment

- Switching of systemic treatment
- Assessment of surrogate biological endpoints
- Advancement of new drug development

Downstaging Axilla

Complete Axillary Response

- Downstaging axilla → 44% becomes lymph node–negative
- Strong prognostic factor



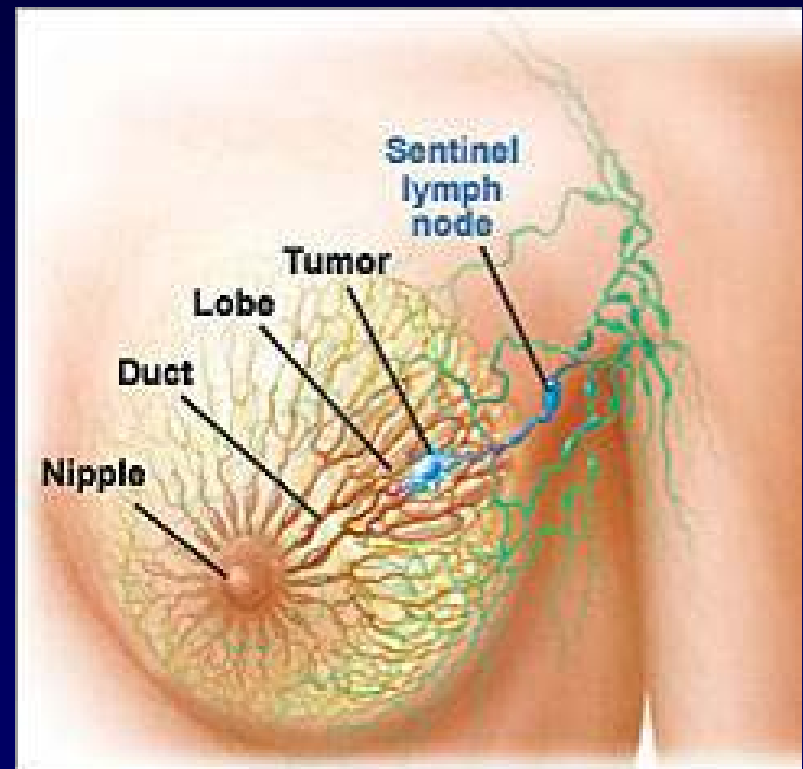
Question 3: Timing of SLNB

<i>Timing</i>	<i>Advantage</i>
Before NAT	<ul style="list-style-type: none">- Accurate information initial status- Sensitivity/specificity clear
After NAT	<ul style="list-style-type: none">- Axillary node dissection prevention after downstaging- 1 instead of 2 operations- No delay in start NAT- Response assessment axilla (prognostic factor)

Question 3: Timing of SLNB

SNLB After NAT

- **Potential disadvantage** → *theory of limited accuracy*
 - Change axillary drainage
 - Destruction of metastases results in fibrosis



Question 3: Timing of SLNB

Sentinel Lymph Node Surgery After Neoadjuvant Chemotherapy is Accurate and Reduces the Need for Axillary Dissection in Breast Cancer Patients.

Hunt KK, Yi M, Mittendorf EA, Guerrero C, Babiera GV, Bedrosian I, Hwang RF, Kuerer HM, Ross MI, Meric-Bernstam F.

From the Department of Surgical Oncology, M.D. Anderson Cancer Center, The University of Texas, Houston, TX

- **Retrospective analysis, N = 3746**
- **Clinically node-negative, T1-3 breast cancer**
- **SLNB in 1994 - 2007**

575 patients (15.3%) neoadjuvant chemo

3171 patients (84.7%) surgery first

Question 3: Timing of SLNB

- Patients receiving neoadjuvant chemotherapy
 - Were younger: 51 years vs 57 years
 - Had larger tumors (T2-3): 87.3% vs 18.8%
 - Had fewer positive SLNs
 - T1: 12.7% vs 19.0%
 - T2: 20.5% vs 36.5%
 - T3: 30.4% vs 51.4%
 - Had similar DFS

Downstaging

	Neoadjuvant	Surgery first
Identification rate	97.4%	98.7%
False-negative rate	5.9%	4.1%

Question 3: Timing of SLNB

Strategies to Increase Sensitivity Identification SLN After NAT

Can Breast MRI Predict Axillary Lymph Node Metastasis in Women Undergoing Neoadjuvant Chemotherapy

Sara Javid¹, Davendra Segara¹, Parisa Lotfi², Sughra Raza³, and Mehra Golshan¹

Feasibility of FDG PET/CT to monitor the response of axillary lymph node metastases to neoadjuvant chemotherapy in breast cancer patients

Marieke E. Straver • Tjeerd S. Aukema • Renato A. Valdes Olmos •
Emiel J. T. Rutgers • Kenneth G. A. Gilhuijs • Margaret E. Schot • Wouter V. Vogel •
Marie-Jeanne T. F. D. Vrancken Peeters

Eur J Nucl Med Mol Imaging (2010) 37:1069–1076

Marking the axilla with radioactive iodine seeds (MARI procedure) may reduce the need for axillary dissection after neoadjuvant chemotherapy for breast cancer

M. E. Straver¹, C. E. Loo², T. Alderliesten², E. J. T. Rutgers¹ and M. T. F. D. Vrancken Peeters¹

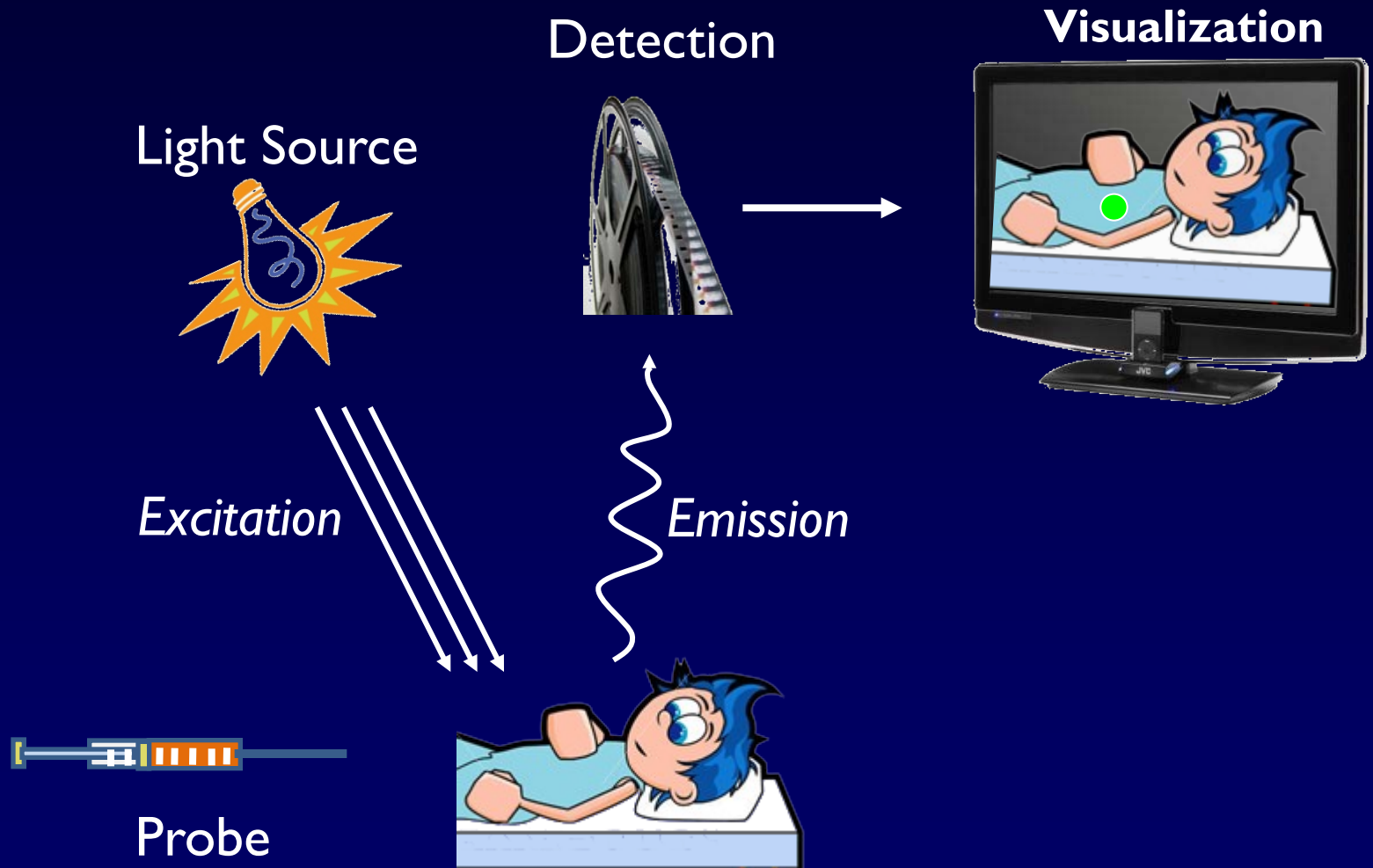
Question 3: Timing of SLNB

Strategies to Increase Sensitivity Identification SLN After NAT

- **Fluorescence imaging**
 - SLN detection with near-infrared fluorescence light
 - Indocyanine green
 - Intraoperative camera system (Frangioni Laboratory, Boston)



Near-Infrared Fluorescence Imaging

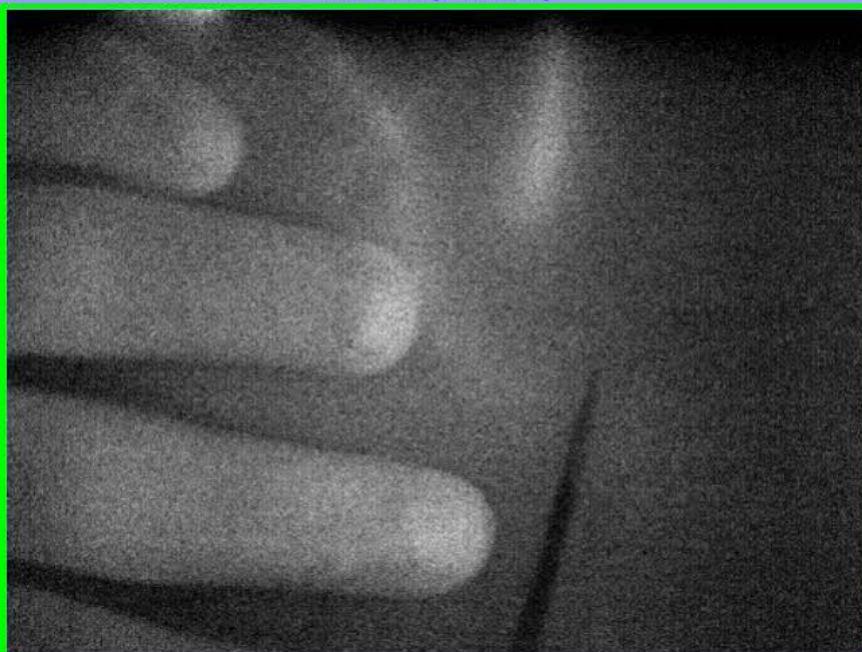




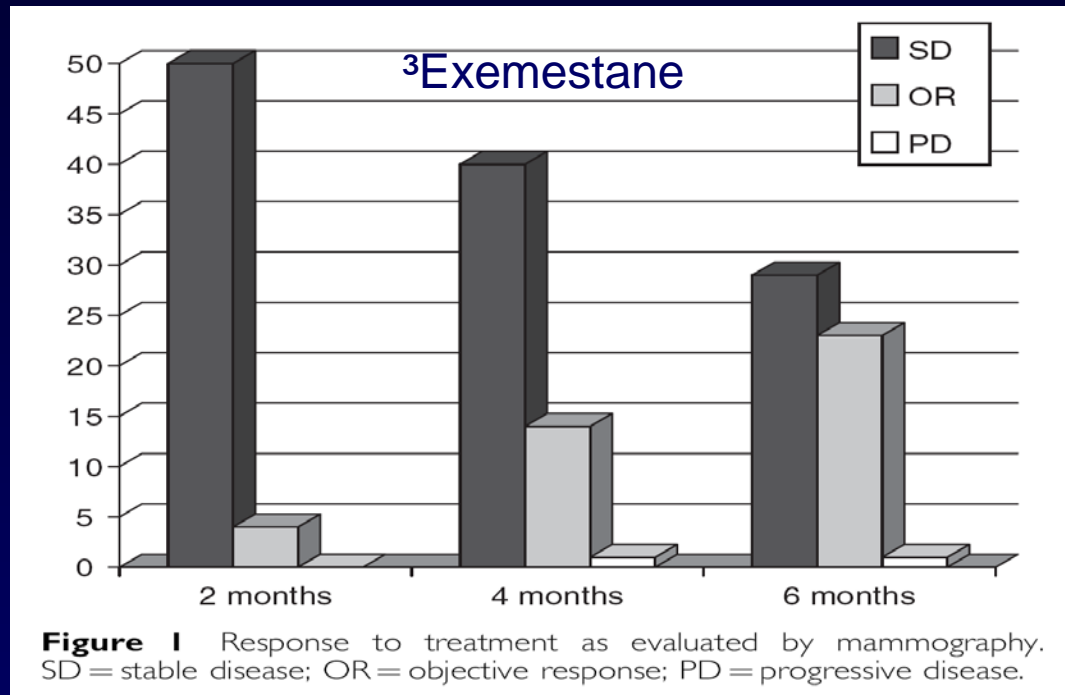
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Question 4: Duration NAT?



² Duration letrozole	% CR
3 months	9.5
6 months	29
12 months	36

¹**Conclusion:** Over half of patients become BCS-eligible within 4 months of preoperative letrozole treatment. While prolonged treatment for up to 8 months can result in further tumor volume reduction in some patients, there is no clear optimum for treatment duration.

My Opinion

- **ER+ patients - neoadjuvant endocrine treatment with AI up to 6 months**
 - **Hormone therapy feasible, especially in elderly / comorbidity**
 - **In study**
- **MRI assessment after 3 months**
 - **Continuation in case of tumor response**
- **SNB after completion of neoadjuvant therapy**