
Value and Safety of SLN in Vulvar Ca

Conservative Conservation

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Premises

- Inguinal nodes need to be removed in vulvar ca!
 - Risk of LN invmt in early vulvar cancer
 - Prognostic sig of LN invmt in vulvar ca
 - Therapeutic value of ILND
 - ILND has significant morbidity
 - Rationale for the SLN concept
 - Clinical evidence for safety and efficacy of SLN in vulvar ca
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Risk for ILN mets in vulvar ca

Depth	n	(+) nodes
< 1 mm	120	0%
1.0-2 mm	121	7%
2.1- 3 mm	97	8%
3.1- 4 mm	50	22%
4.1-5 mm	40	25%
> 5 mm	32	38%
		Total: ~30%

Risk for ILN mets in vulvar ca

Thickness	n	%
< 1 mm	1/32	3%
2 mm	5/56	9%
3 mm	11/59	19%
4 mm	21/68	31%
5 mm	19/57	33%
>5 mm	137/286	48%

Sedlis et al, GOG36, AJOG 1987
Homesley et al, GOG36, Gyn Onc 1993

Superficial: 20%

Risk for ILN mets in vulvar ca

Other risk factors for nodal spread:

- Age: 45% > 75yrs
- Tumor size (clinical and pathological)
- Tumor grade

■ CLSI / LVSI

In superficial vulvar ca

CLSI	(+) nodes	2 or more (+) nodes
(+)	65%	40%
(-)	17%	8%

Sedlis et al, GOG36, AJOG 1987

Homesley et al, GOG36, Gyn Onc 1993

Prognostic fx in vulvar ca

■ Margins

Heaps J, Gynecol Oncol 38(3):309, 1990

□ Margin status (n=135)

■ > 8 mm = 0% recur;

■ < 8 mm = **50% recur**

Chan J, Gynecol Oncol 104(3):636, 2007

■ > 8 mm = 0% recur

■ < 8 mm = **23% recur**

■ LVSI

Heaps J, Gynecol Oncol 38(3):309, 1990

X4 local recurrence for LVSI (+)

Sedlis et al, GOG36, AJOG 1987

X4-5 LN mets for LVSI (+)

Prognostic fx in vulvar ca

■ Node status is the most important prognostic fx in vulvar ca!

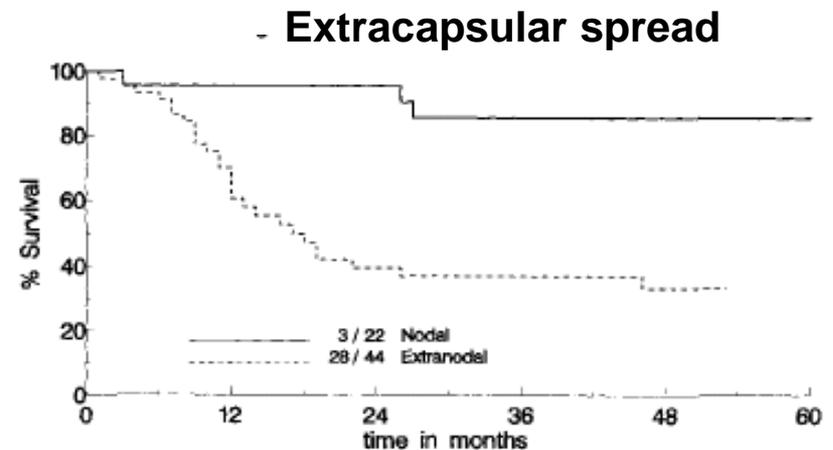
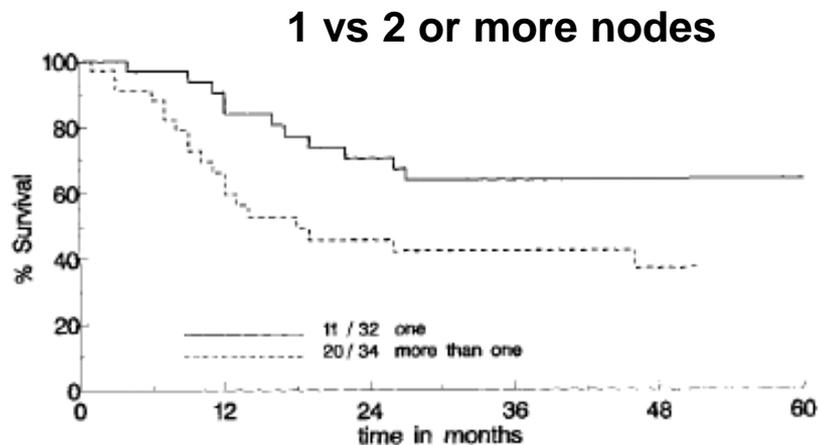
Hacker Obst Gyn 61:408, 1983, survival in vulvar ca pts

- **N0 96%**
- **N1 56% (94% for 1 node, 80% for 2 nodes, 12% for 3 or more)**

Homesely AJOG 164(4):997, 1991 5-year-survival for four risk groups:

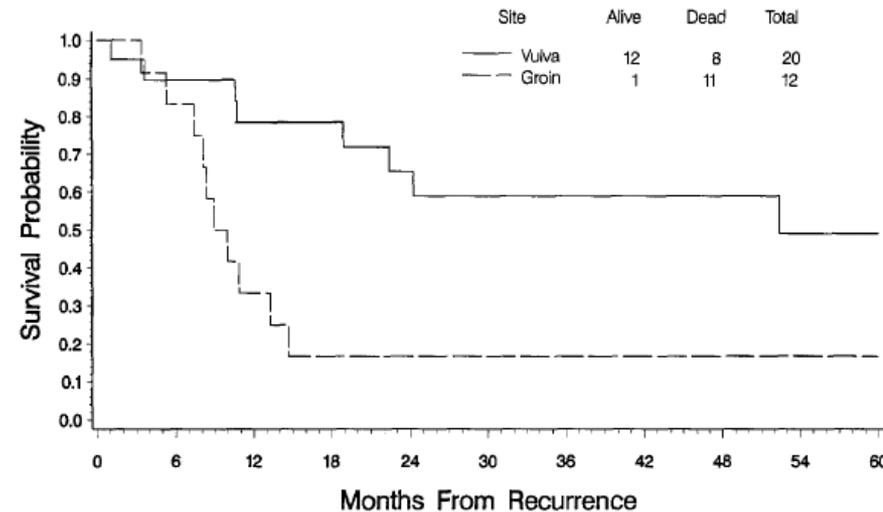
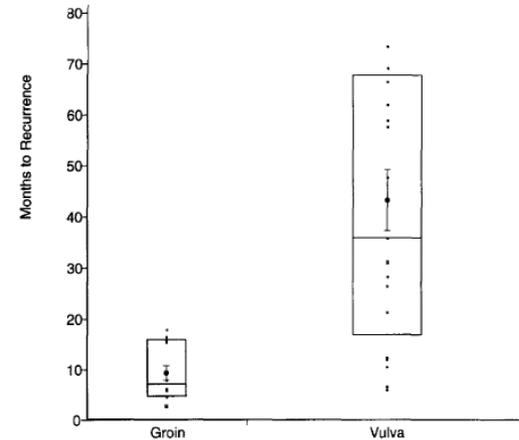
- tumor < 2 cm and (-) nodes - 98%
- tumor < 2 cm and 1 node (+) or tumor 2-8 cm with (-) nodes - 87%
- tumor 2-8 cm with (+) nodes or tumor > 8 cm - 75%
- **3 (+) nodes or bilaterally (+) nodes - 29%**

Van der Velden Cancer 75(12):2885, 1995



Therapeutic value of ILND

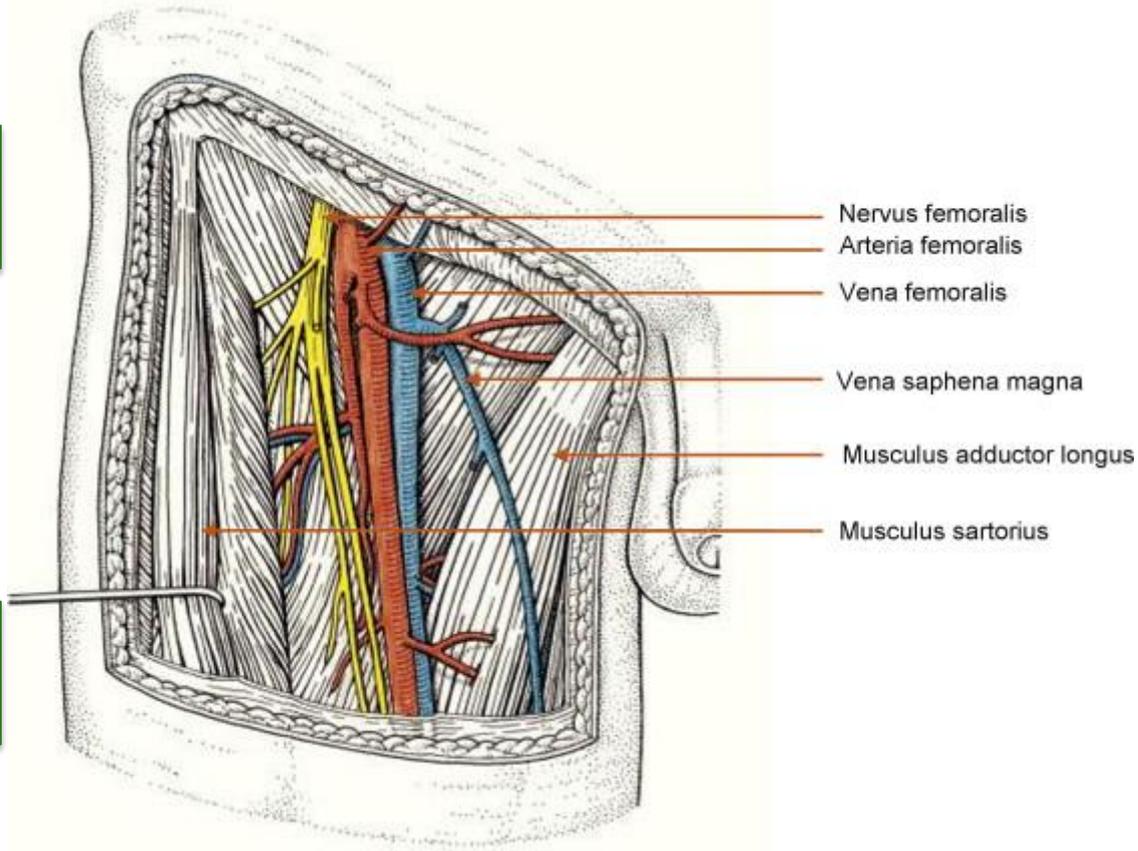
	Groin dissection	Groin radiation
Vulvar rec	4%	4%
Groin rec	0%	19%
DOD	4%	26%



Inguinal Lymphadenectomy

Superficial: above cribriform fascia

Deep: below cribriform fascia



Inguinal lymphadenectomy

- Superficial vs. deep ILND:
 - Groin recurrences after superficial ILND are @ 5-9% across studies with lower complication rates
 - no head-to-head trials!

- Unilateral vs. bilateral ILND:
 - Safe in small, lateralized, lesions
 - <1% contralateral node metastases with neg unilateral groin nodes

Stehman, Gynecol Oncol 2009

Gordinier, Gynecol Oncol 2003

Kirby, Gynecol Oncol 2005

Burke, Gynecol Oncol 1995

Stehman, Obstet Gynecol 1992

Morbidity of ILND

Stehman, Obstet Gynecol 79:490, 1992

Rouzier, J Am Coll Surg 196:442, 2003

Gaarenstroom IJGC 13:522, 2003

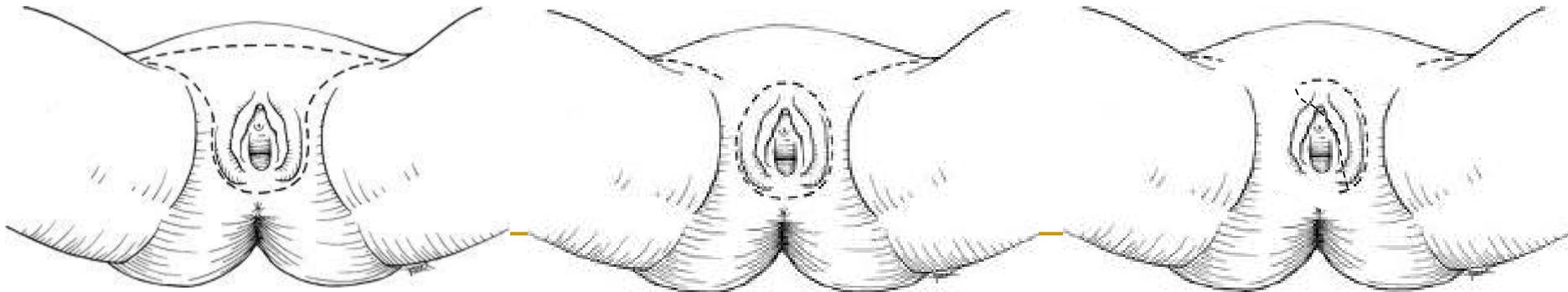
Van Der Zee JCO 26:884, 2008

Hinten, BJC 105:1279, 2011

	%
Breakdown	11-19%
Infection	27-29%
Lymphocyst	27-29%
Hematoma	2%
Lymphedema	20-40%
Rec erysipelas / cellulitis	15-30%

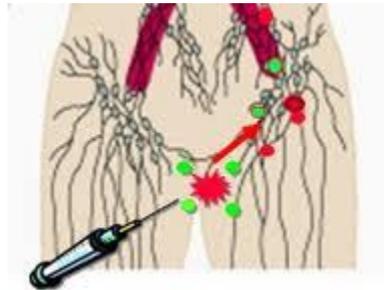
Modifications in treatment

- The goal of any modification in treatment is to improve morbidity and QOL without compromising oncological safety
 - Surgery in separate incisions
 - Radical local excision in small lateralized tumors
 - Omission of ILND in microinvasive tumors
 - The SLN procedure



The sentinel node concept

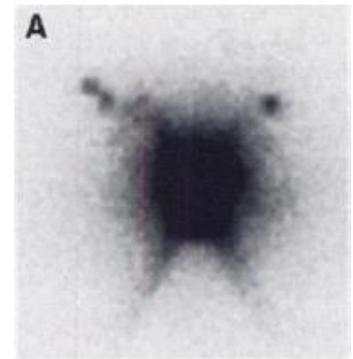
- The first draining lymph node in a lymphatic basin that receives primary lymph flow from a tumor
- Represents the pathology of all lymph nodes in that basin



- First described in parotid gland tumors, then penile cancer
- Now state-of-the-art treatment for malignant melanoma (>99% sensitivity) and breast cancer (96% sensitivity)

SLN in vulvar ca - technique

- Intradermal peritumoral injection of ^{99}Tc -labelled nanocolloid
- Particle size determines rate of spread and impacts timing of injection
- Lymphoscintigraphy to identify SLN in each targeted groin pre-operatively
- Intraoperative injection of blue dye
- Identification of SLN:
 - visualization of lymphatic drainage (blue)
 - use of gamma probe to detect radioactive foci in the groin bed and confirm correct identification of SLN after removal



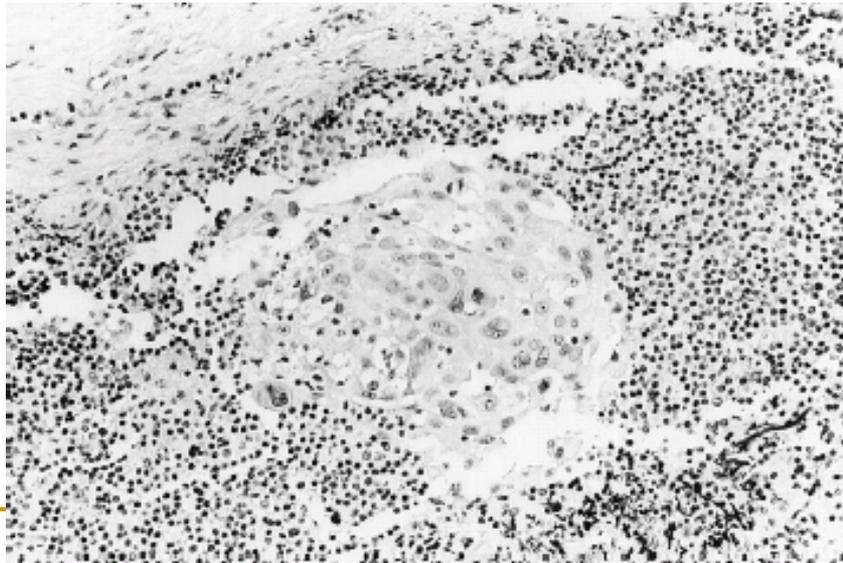
SLN in vulvar cancer - prerequisites

- Resectable tumors
 - Invasion > 1mm
 - No clinically suspicious nodes
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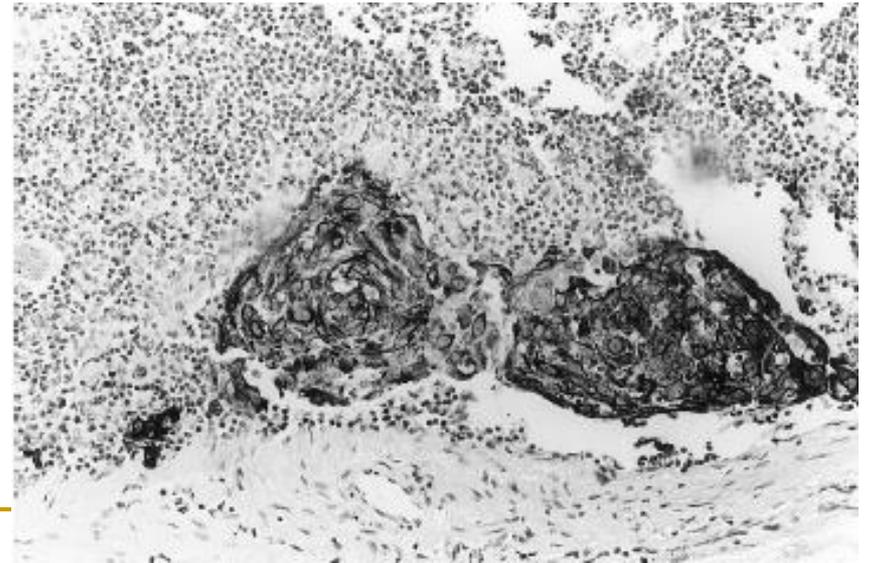
SLN in vulvar ca - advantages

- Decreases morbidity of ILND
- Higher detection rates of micrometastases with ultrastaging (4% FN of standard histology)

De Hullu, JCO 18:2811 2000



Micrometastasis found on step sectioning



Micrometastasis found on cytokeratin staining

Accuracy of SLN in vulvar ca

study	N	injection	Path	Detection	(+) SLN	(+)nodes	Sens	NPV	FN
Van Der Zee 2000	59	RC + BD	Ultra-staging	100% lat 88% med	39%	39%	100%	100%	0%
Levenback 2001	52	BD only	variable	88% lat 69% med	19%*	21%	100%	100%	0%
Hauspy 2007	41	RC + BD	Ultra-staging	85%	39% (2% US)	39%	100%	100%	0%
HAMPL 2008	127	RC + BD	Ultra-staging	98%	28%	31%	92%	97%	8%
Vidal 2007	62	RC + BD	Ultra-staging	88%	17%	17%	100%	100%	0%
Rob 2007	59	RC + BD	Ultra-staging	86%	21%	22%	95%	99%	5%
Lindell 2010	77	RC + BD	Ultra-staging	72%	17%	19%	92%	98%	8%

All studies **1398**

98%

8%*

Accuracy of SLN in vulvar ca

Levenback, JCO 30:3786-3791, 2012

Table 2. SLNB Sensitivity Analysis

Analysis	SLNB Result	Lymph Node Metastasis			Statistics					
		Present	Absent	Total	Sensitivity	90% CI	NPV (%)	90% CI	FNPV (%)	90% CI
By patients	Positive	121	0	121	91.7	88.7 to 95.3	96.3	93.9 to 97.9	3.7	2.1 to 6.1
	Negative	11	286	297						
	Total	132	286	418						
By groin	Positive	140	0	140	92.1	87.5 to 95.4	97.4	95.7 to 98.5	2.7	1.5 to 4.3
	Negative	12	441	453						
	Total	152	441	593						
In tumors < 4.0 cm	Positive	67	0	67					2.0	0.7 to 4.5
	Negative	4	198	202						
	Total	71	198	269						
In tumors ≥ 4.0 cm	Positive	54	0	54					7.4	3.5 to 13.4
	Negative	7	88	95						
	Total	61	88	149						

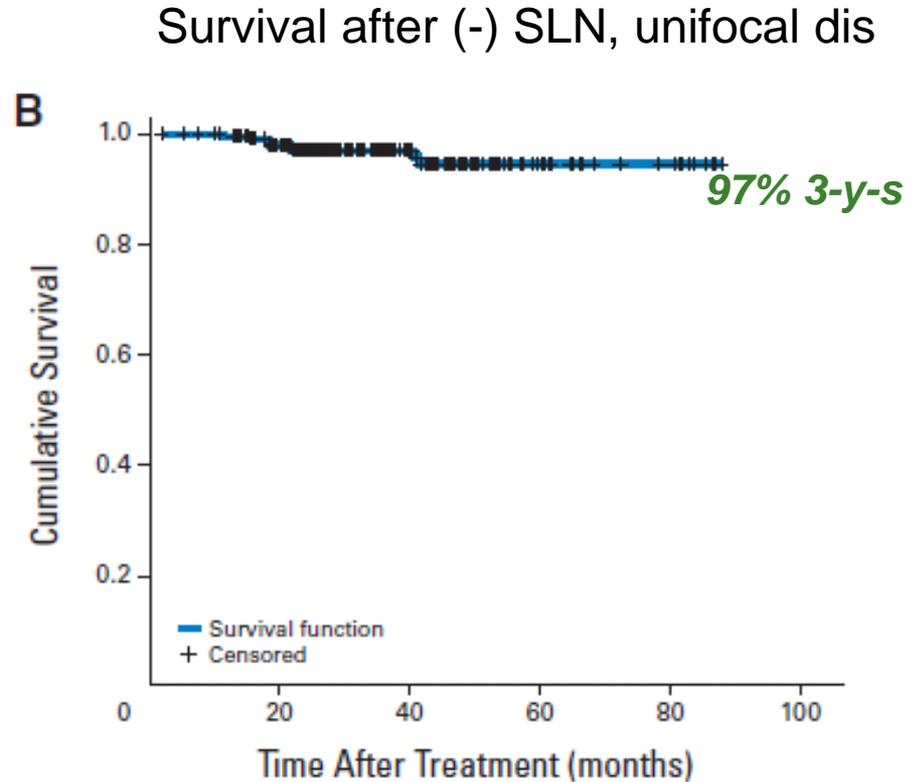
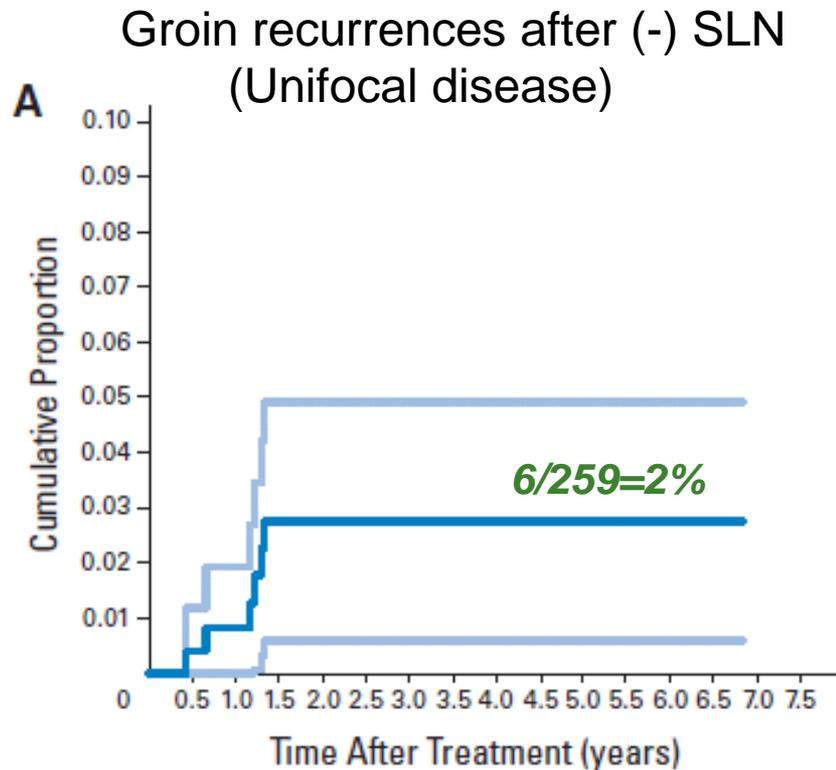
Abbreviations: FNPV, false-negative predictive value; NPV, negative predictive value; SLNB, sentinel lymph node biopsy.

NPV=97%

FN=8%

Efficacy of SLN in vulvar ca

Van Der Zee, JCO 26:884, 2008



Morbidity data, SLN vs ILND

Van Der Zee, JCO 26:884, 2008

	SLN	SLN + ILND
Hospital stay	8d	14d
wound breakdown	12%	34%
cellulitis	5%	21%
Lymphedema	2%	25%
Rec erysipelas	0.4%	16%

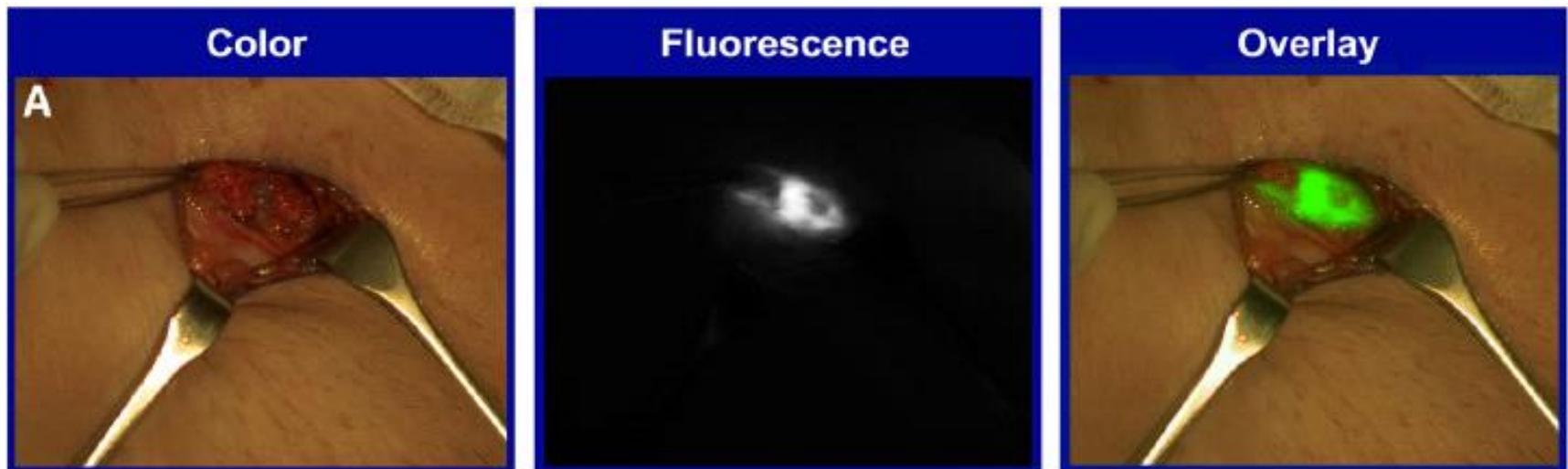
p<0.001

Pitfalls in SLN for vulvar ca

- Injectable agent: radiocolloid, dye or both?
- Timeline / schedule: changes with particle size.
- Collaborative three team effort: requires
 - standardization of injection technique
 - timing of surgery
 - tailored pathological processing and interpretation
- Learning curve (10-30 cases) *Morton 1999, Cody 1999, Levenback 2001*
- Intra-operative decision to extend groin dissection depends on FS evaluation of SLN (15/16=94% detection rate, *Hauspy Cancer 110:1015, 2007*)
- SLN after excisional biopsy? Lower SLN detection rate but probably no compromise in accuracy and outcome
Levenback Gyn Onc 83:276, 2001; Woelber Ann Surg Oncol 20:1701, 2013

Future directions

- Intraoperative Fluorescent Imaging for SLN detection, *Crane, van der Zee Gyn Oncol 2011*



- Continuous real-time imaging
- 90% detection rate compared to radiocolloid

Summary and conclusions

- Evaluating groin status is of cardinal importance in the treatment of vulvar ca because
 - A significant proportion of patients have groin mets even w superficial tumors
 - LN status is the most significant factor impacting prognosis
 - Groin recurrences are nearly always fatal, and lymphadenectomy performs better than radiation in preventing it
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Summary and conclusions

- ILND carries significant patient morbidity which may be largely avoided with SLN
 - The SLN procedure is safe and accurate in determining nodal status with an acceptable (<5%) FN rate (close to 0 in experienced centres)
 - The SLN procedure requires a collaborative effort in a dedicated centre and has a clinically important learning curve
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THANK YOU!

