Bases du traitement chirurgical du cancer bronchique

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DES de Pneumologie Ile-De-France

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Buts de la présentation

1. Bases oncologiques de la chirurgie
2. Bases fonctionnelles
3. Indications
4. Déroulement
5. Résultats attendus

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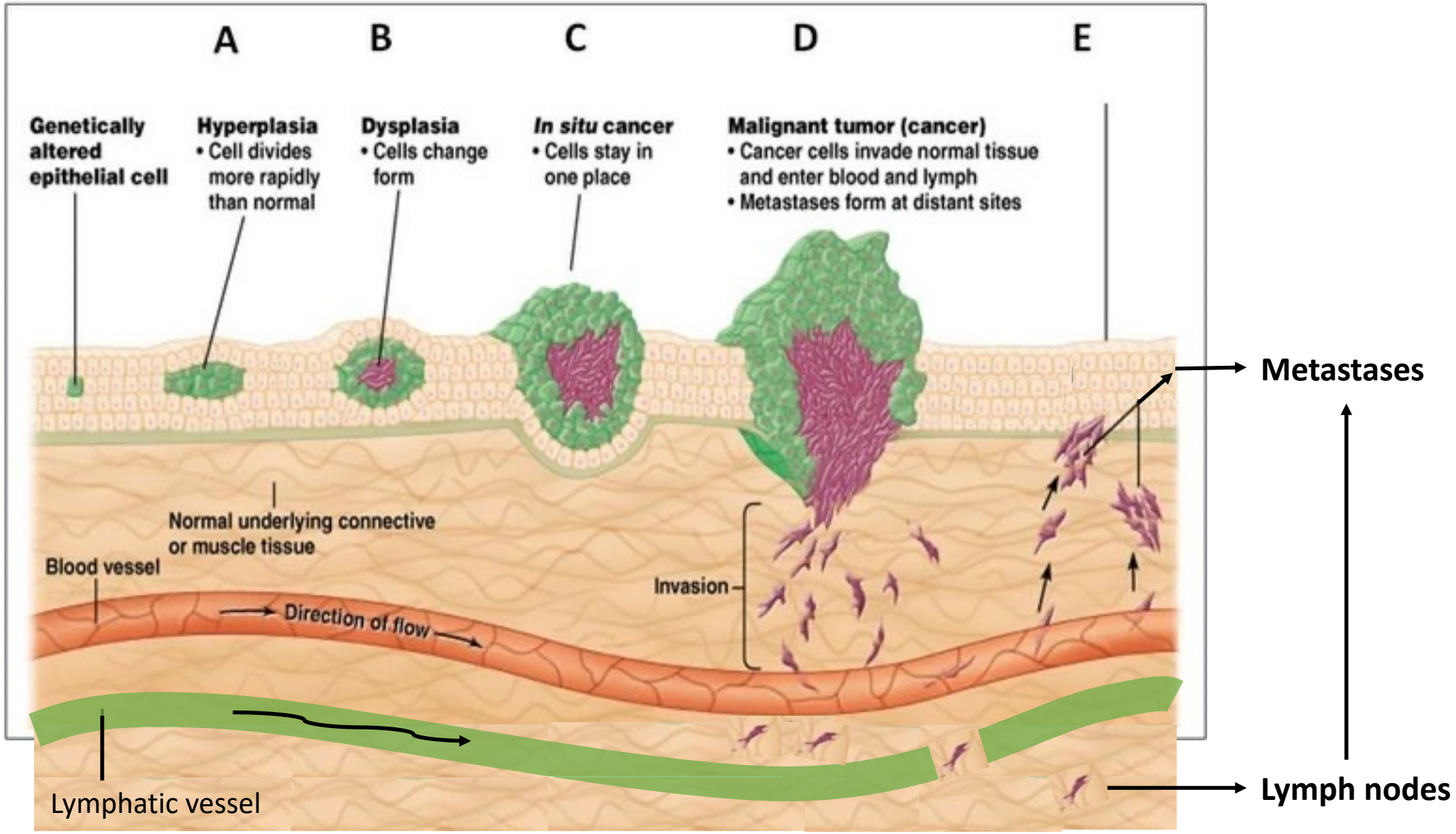
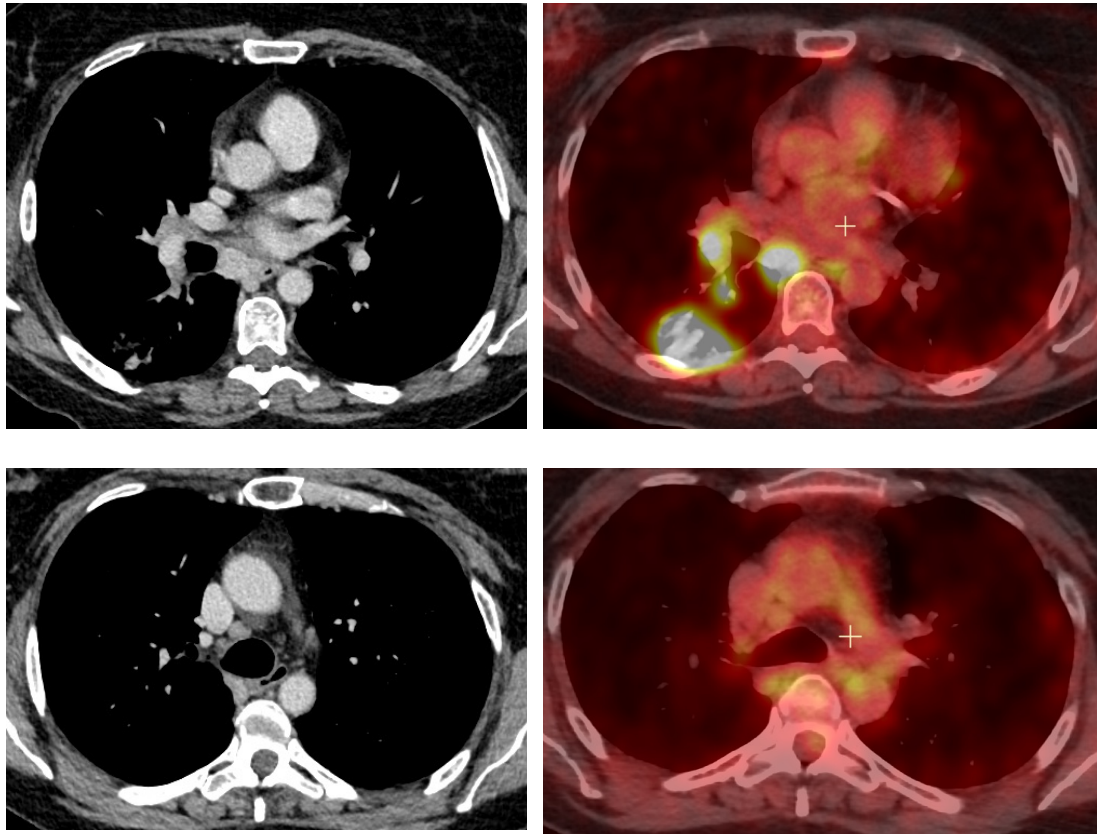
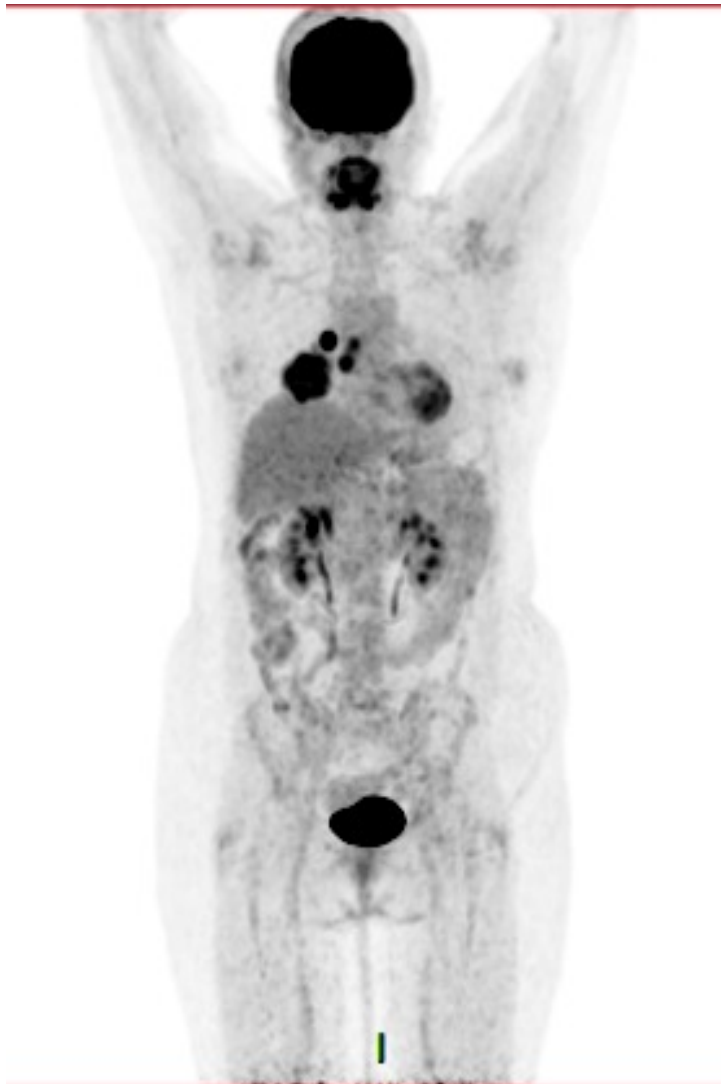
Progression tumorale



Extension ganglionnaire

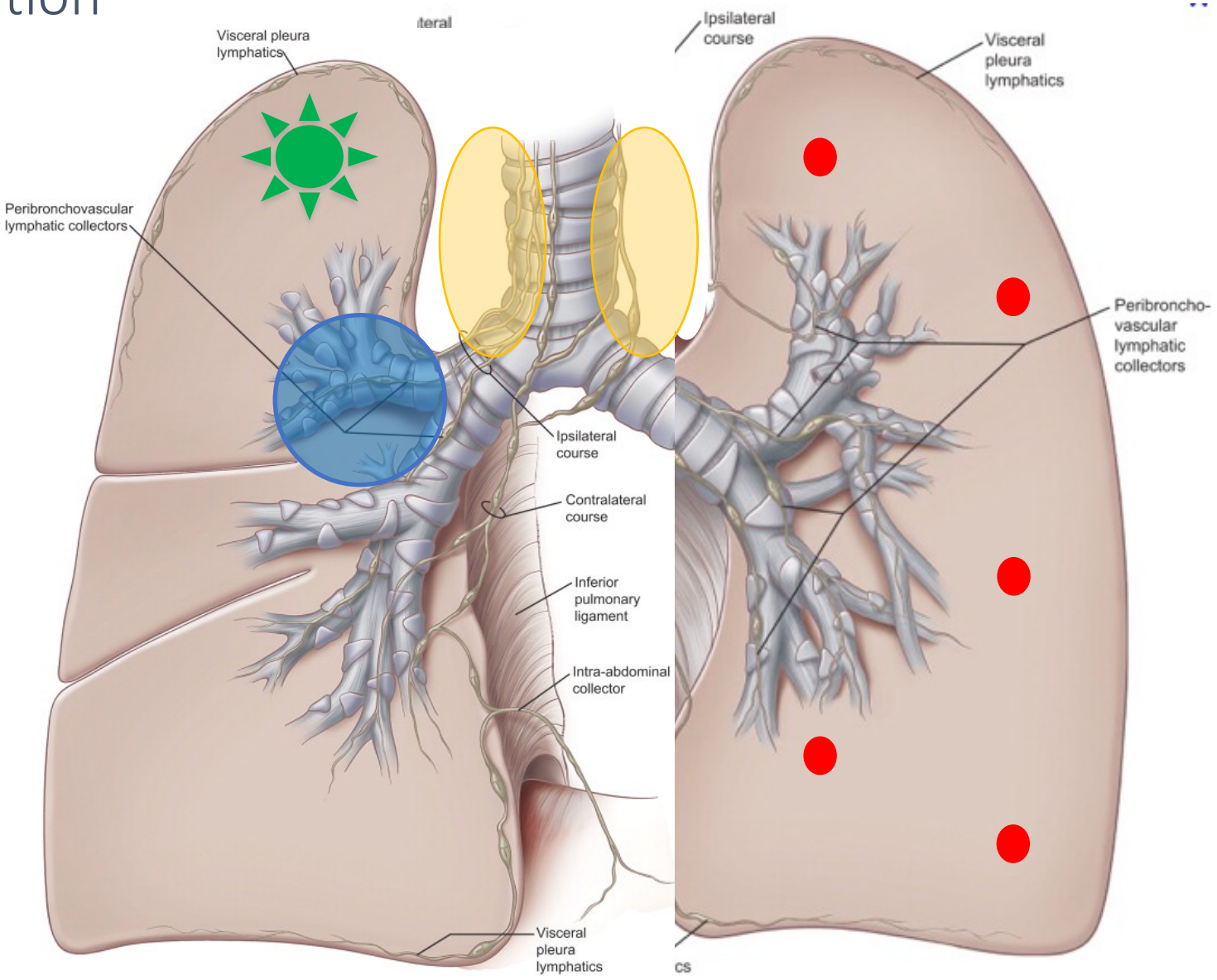




Stadification

Stage I

Stage II



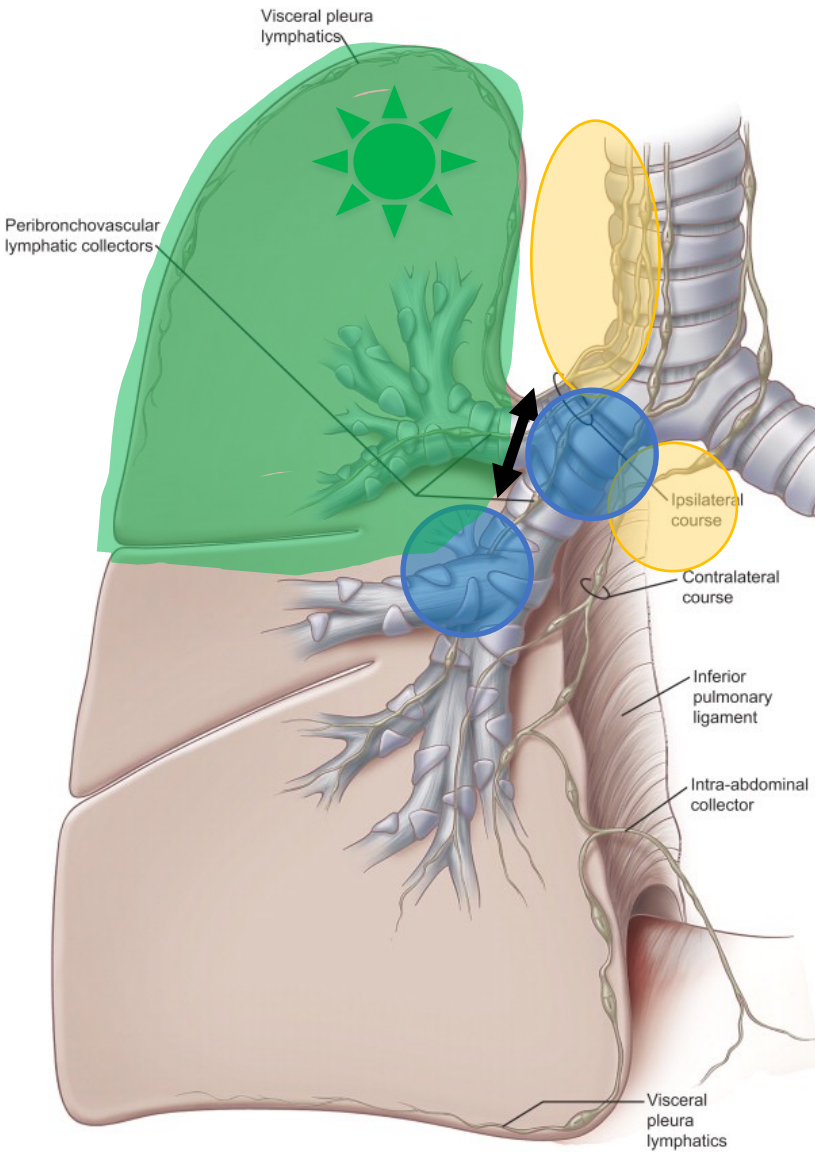
Stage III

Stage IV

Bases de la chirurgie oncologique

Complete resection
- Tumor
- Anatomical segment
- Vessels + bronchus
- Adequate margins

Lymph node management
- SLN Dissection



Résections pulmonaires

Résections anatomiques

(dites « réglées »)

Pneumonectomie

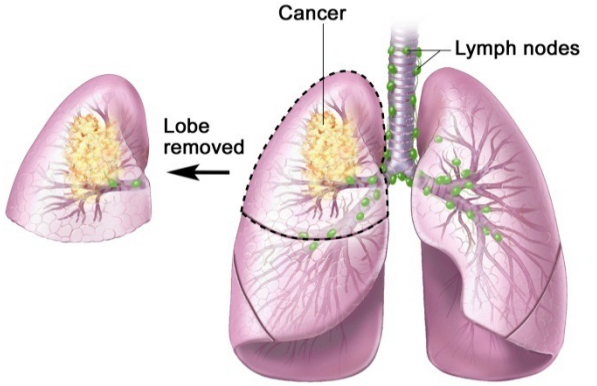
Lobectomie

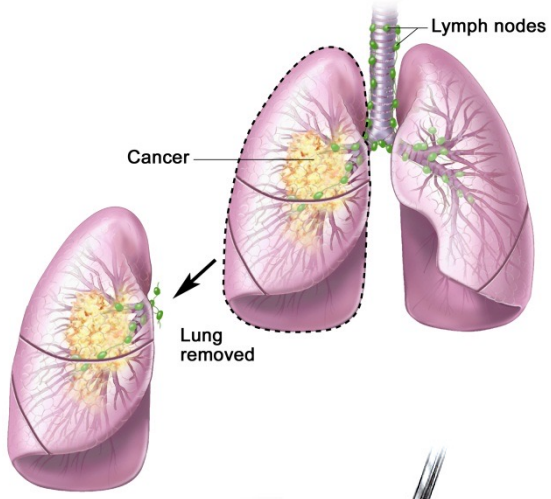
Segmentectomie

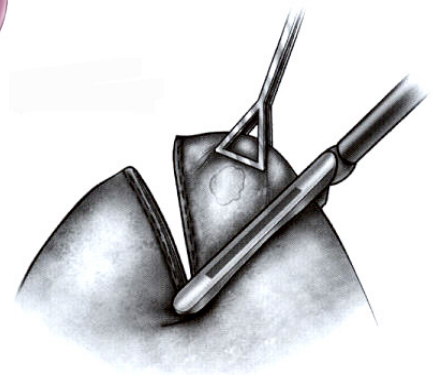
Résections non anatomiques

(dites « atypiques »)

= wedges







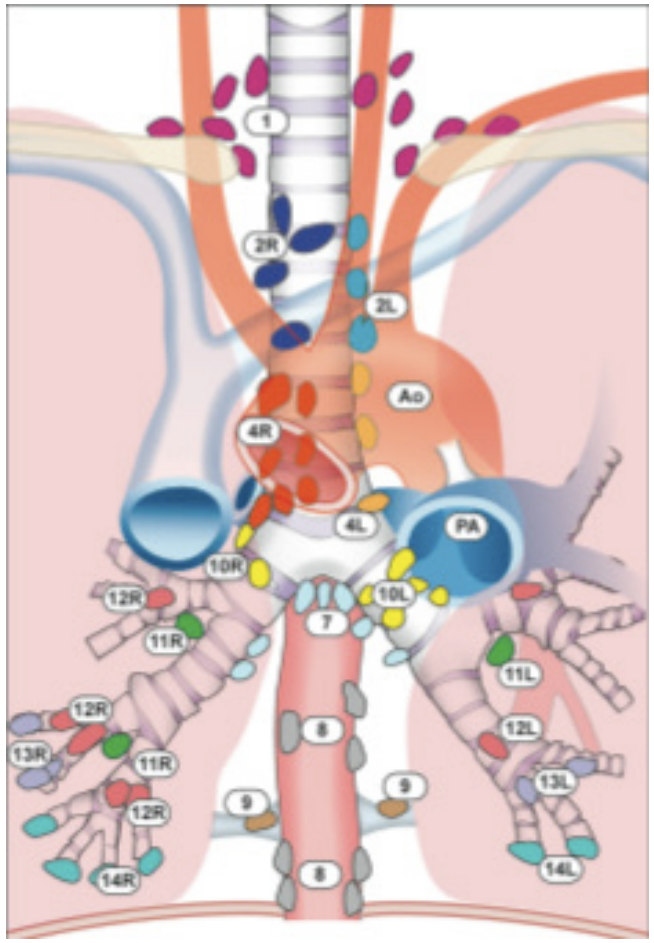
Curage ganglionnaire

- Intrapulmonaire: 11, 12
- Hilaire: 10

= 3 zones N1

- Médiastinal inf : 8-9, 7
- Médiastinal sup: 4R ou 5-6

= 3 zones N2



Bases oncologiques de la chirurgie

1. Résection anatomique: segment, lobe, bilobe, poumon

2. Emportant la tumeur et son drainage lymphatique
- intra parenchymateux et hilaire => 3 zones N1
- Médiastinal => 3 zones N2

3. Avec des marges satisfaisantes
- Recoupe bronchique saine
- Recoupes vasculaires saines
- Résection R0

Pourquoi faut-il faire une résection anatomique/curage ?

Table 1: Clinicopathologic characteristics ($n = 1667$)

Characteristic	Number	%
Sex		
Male	681	41
Female	986	59
Age, years, median (range)	69 (28–89)	
≤70	944	57
>70	723	43
Laterality		
Right	1094	66
Left	573	34
Location		
Right upper lobe	474	28
Right middle lobe	59	4
Right lower lobe	452	27
Left upper lobe	400	24
Left lower lobe	282	17
Median diameter of lesion, cm (range)	2.3 (0–14)	
Size 0–2 cm	743	45
Size 2.1–4 cm	694	42
Size >4 cm	228	14
Missing	2	0.1
Median SUVmax (range)[a]	4.65 (0–42)	
Surgical approach		
VATS	487	29
Open	1180	71
Type of resection		
Wedge resection	139	8
Segmentectomy	199	12
Lobectomy	1329	80
Pathological N status		
N0	1384	83
N1	137	8
N2	146	9
Histology		
Adenocarcinoma	738	44
Lepidic-predominant	548	33
Squamous	269	16
Other	113	7

MSKCC 2000-2012
1667 patients cStage I
CT, TEP-CT, opérables

↓

Résection anatomique primitif
+ curage systématique

↓

Pas de mortalité postopératoire

↓

83% N0
9% N1
8% N2
(dont 34% skip et 16% croisé)

Bille et al, EJCTS 2017

Pourquoi faut-il être R0 ?

VA 2006-2016
9628 patients cStage I
CT, TEP-CT, opérables

↓

Résection chirurgicale

↓

Chirurgie / 12 semaines
Abord ouvert / vidéo
Etendue de la résection
(Nombre de gg)
R0 / R+

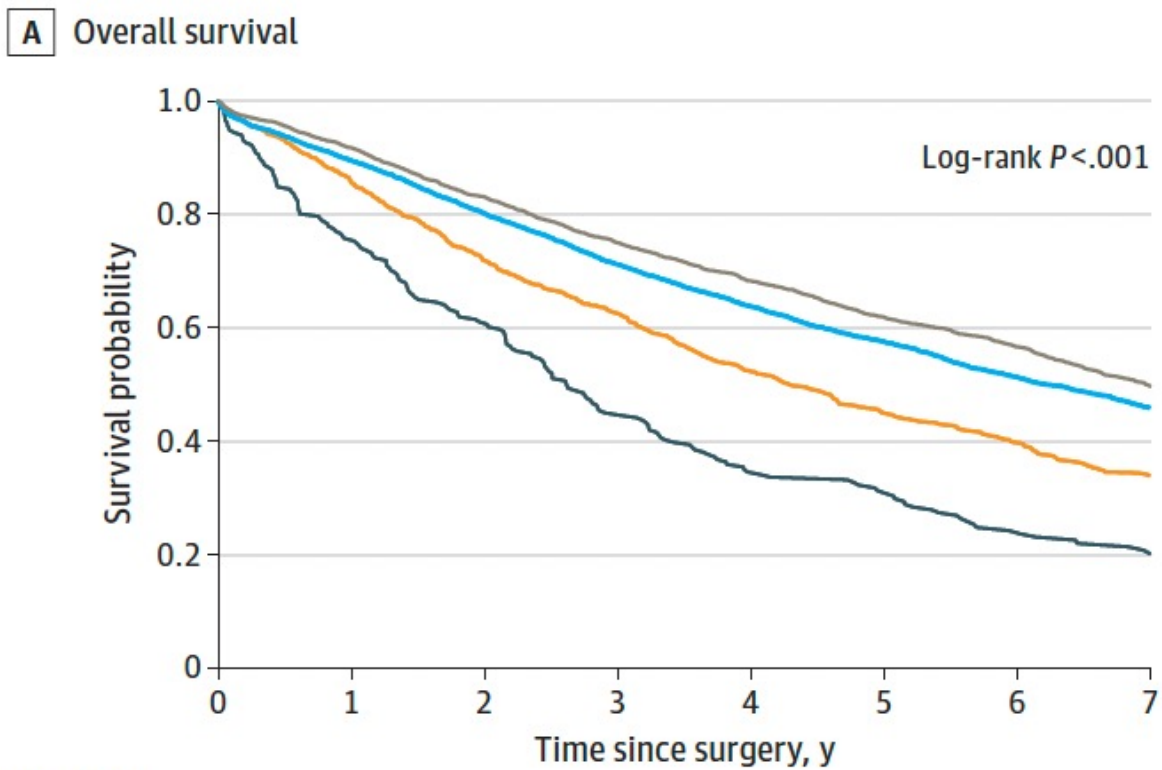
↓

Score de qualité de la chirurgie / sur la survie globale

Table 2. Development of the VALCAN-O Score

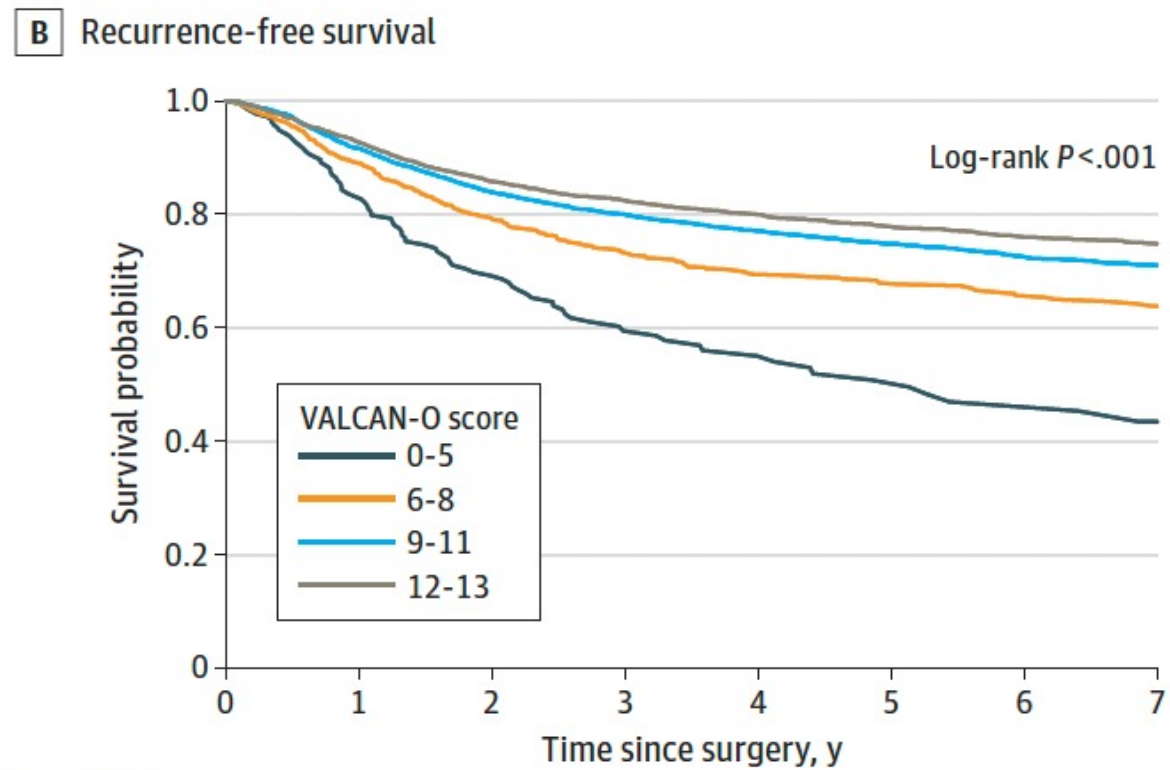
Variable[a]	aHR (95% CI)	β	*P* value	VALCAN-O points
Delayed surgery				
>12 wk	1 [Reference]			0
≤12 wk	0.89 (0.84 to 0.94)	−0.12	<.001	1
Surgical approach				
Open	1 [Reference]			0
Minimally invasive	0.92 (0.87 to 0.97)	−0.09	.003	1
Extent of resection				
Wedge	1 [Reference]			0
Lobectomy	0.83 (0.77 to 0.89)	−0.19	<.001	2
Segmentectomy	0.82 (0.72 to 0.94)	−0.19	.004	2
Pneumonectomy[b]	1.08 (0.88 to 1.34)	0.08	.47	0
Nodal sampling adequacy, LNs				
0	1 [Reference]			0
1-4	0.88 (0.89 to 0.96)	−0.13	.008	1
5-9	0.82 (0.74 to 0.90)	−0.20	<.001	2
≥10	0.78 (0.70 to 0.86)	−0.25	<.001	3
Surgical margin[c]				
R1+	1 [Reference]			0
R0	0.58 (0.51 to 0.67)	−0.54	<.001	6

Heiden et al, JAMA Surg 2023



No. at risk

0-5	231	175	141	104	78	63	44	0
6-8	983	843	707	615	492	370	283	0
9-11	5030	4504	4036	3583	3062	2471	1960	0
12-13	3343	3067	2779	2507	2105	1587	1199	0



No. at risk

0-5	231	149	112	74	56	44	30	0
6-8	983	766	608	504	389	290	213	0
9-11	5030	4180	3540	3096	2627	2088	1635	0
12-13	3343	2875	2494	2220	1857	1381	1026	0

Heiden et al, JAMA Surg 2023

Perspectives

TABLE 4] N Subclassification

Category	Subclass	Description
Nx		Regional lymph nodes cannot be assessed
N0		No regional lymph node involvement
N1	N1a	Single-station N1 involvement
	N1b	Multiple-station N1 involvement
N2	N2a1	Single-station N2 without N1 involvement (skip)
	N2a2	Single-station N2 with N1 involvement
	N2b	Multiple-station N2 involvement
N3		N3 lymph node involvement

Detterbeck *Chest* 2017

Résection R	Définitions
R0	Marges vasculaires, bronchiques, périphérie des structures réséquées en bloc histologiquement saines
R1	Marges histologiquement non saines Cytologie d'un épanchement pleural ou péricardique positive
R2	Résidus tumoraux ou ganglionnaires macroscopiques laissés en place

Notion de <u>résection incertaine</u>

Survie plus faible que les patients R0 et plus élevée que les R1.

Définition :

- moins de 3 stations N1 ou moins de 3 stations N2 systématique
- moins qu'un curage ganglionnaire "lobe-spécifique" systématique
- envahissement de la station ganglionnaire la plus haute dans le médiastin
- présence de carcinome in situ sur la tranche de section bronchique

Edwards *JTO* 2020

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Bases fonctionnelles

PS

Fragilité / oncogériatrie

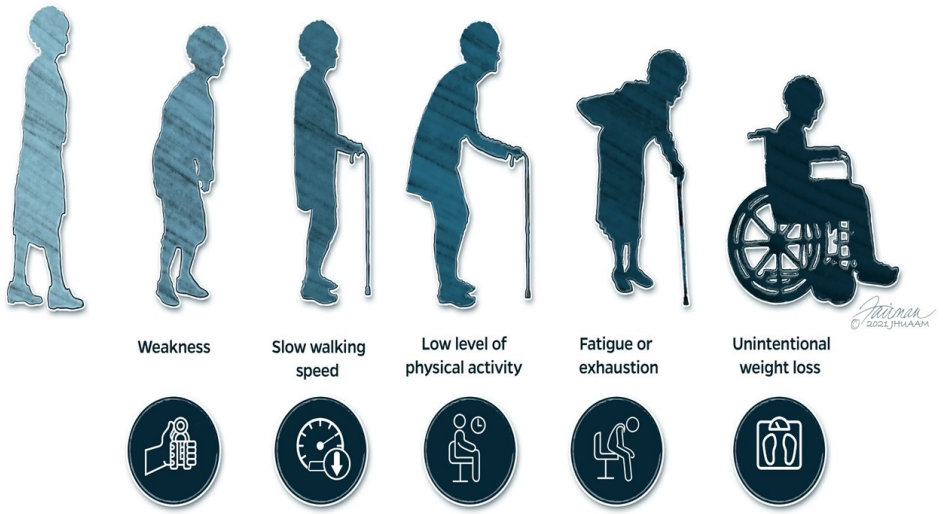
Explorations fonctionnelles respiratoires

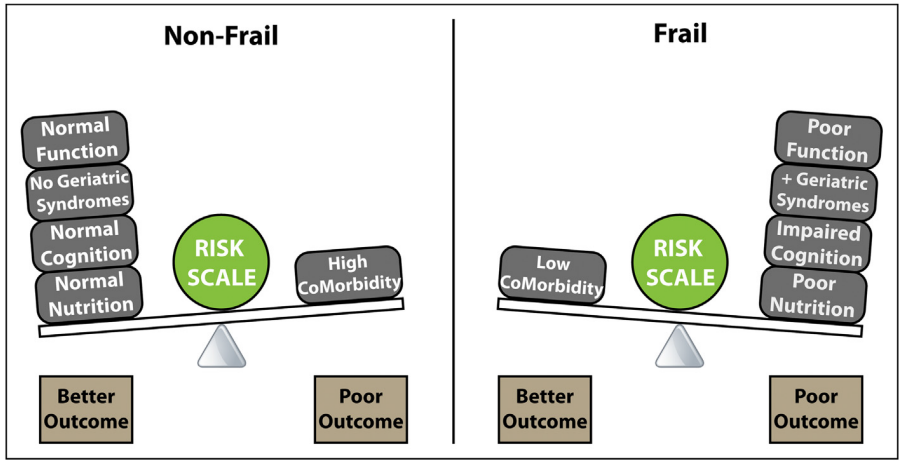
Explorations cardiaques

Etat général

Performance Status Scales

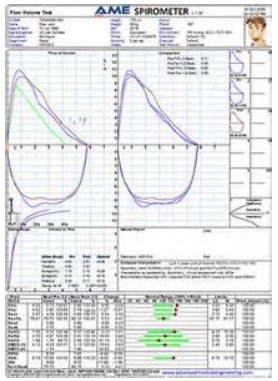
Zubrod Scale		Karnofsky Scale	
0	Normal activity	100	Normal; no evidence of disease
		90	Able to perform normal activities with only minor symptoms
1	Symptomatic and ambulatory; cares for self	80	Normal activity with effort; some symptoms
		70	Able to care for self but unable to do normal activities
2	Ambulatory >50% of time; occasional assistance	60	Requires occasional assistance; cares for most needs
3	Ambulatory ≤50% of time; nursing care needed	50	Requires considerable assistance
		40	Disabled; requires special assistance
		30	Severely disabled
4	Bedridden	20	Very sick; requires active supportive treatment
		10	Moribund





Evaluation pulmonaire

- Explorations fonctionnelles respiratoires
  - VEMS post-op > 1L ou 33% théorique
  - Exérèse mieux tolérée si PaCO2 < 45 et PaO2 > 65 mmHg



- Scintigraphie pulmonaire de ventilation/perfusion

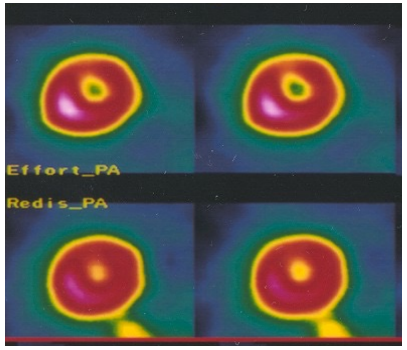
  - meilleure estimation de la fonction postopératoire prédite

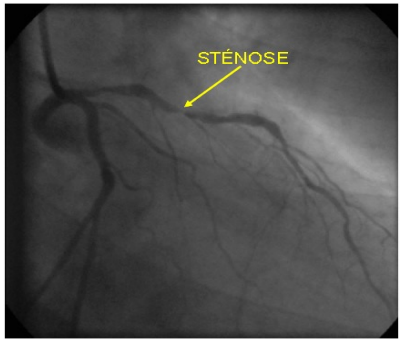
- Si fonction limite,

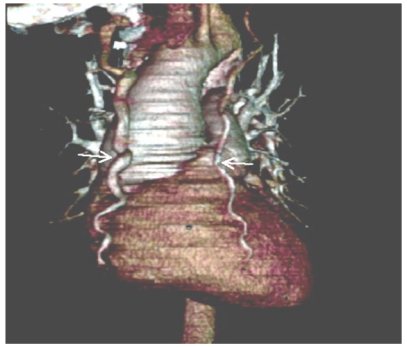
Ne pas hésiter à préparer les patients (sevrage tabac, kiné, bronchodilatateurs…)
Réevaluer après préparation (nouvelles EFR + EFx)

Evaluation cardiaque

- ECG
- Echographie cardiaque
- +/- épreuve d'effort ou scintigraphie myocardique
- +/- Coronarographie

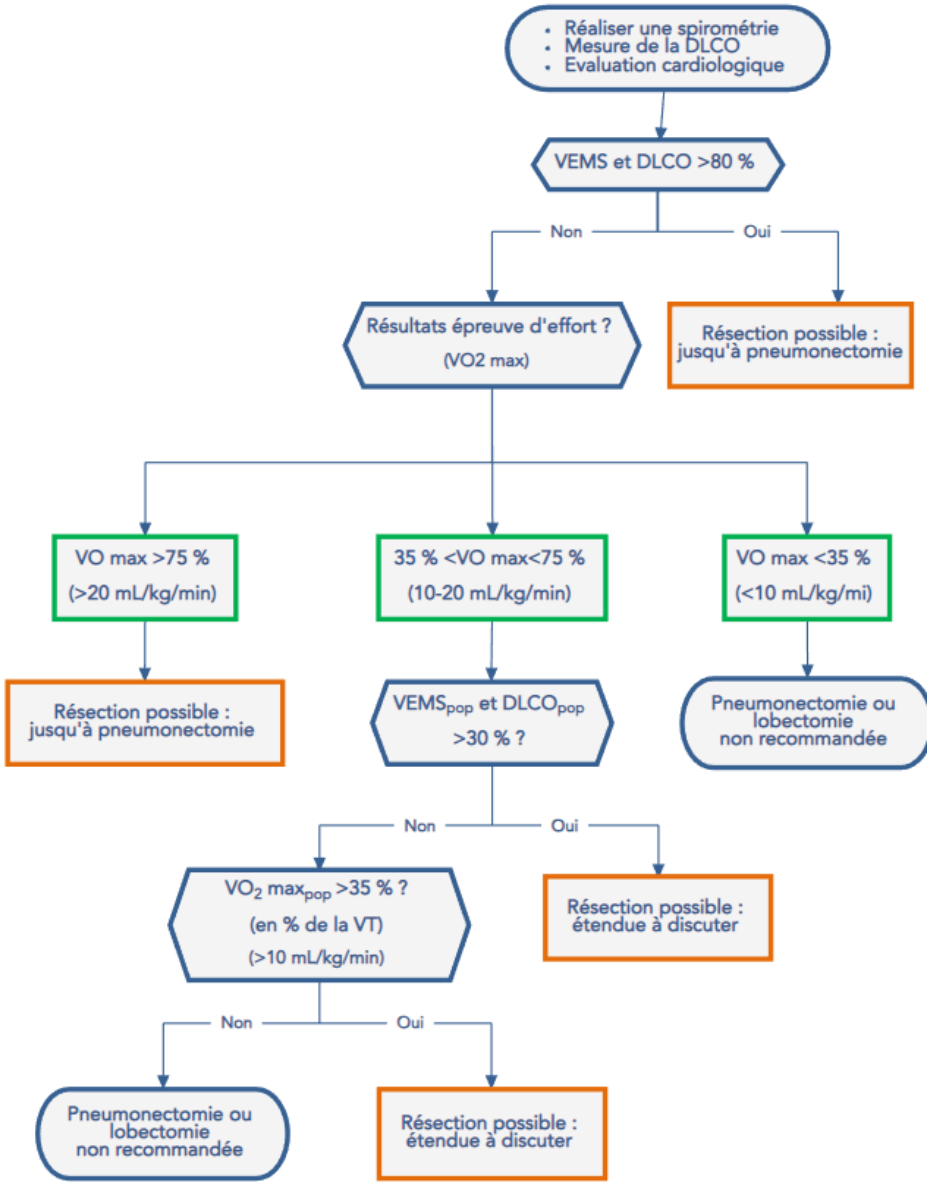




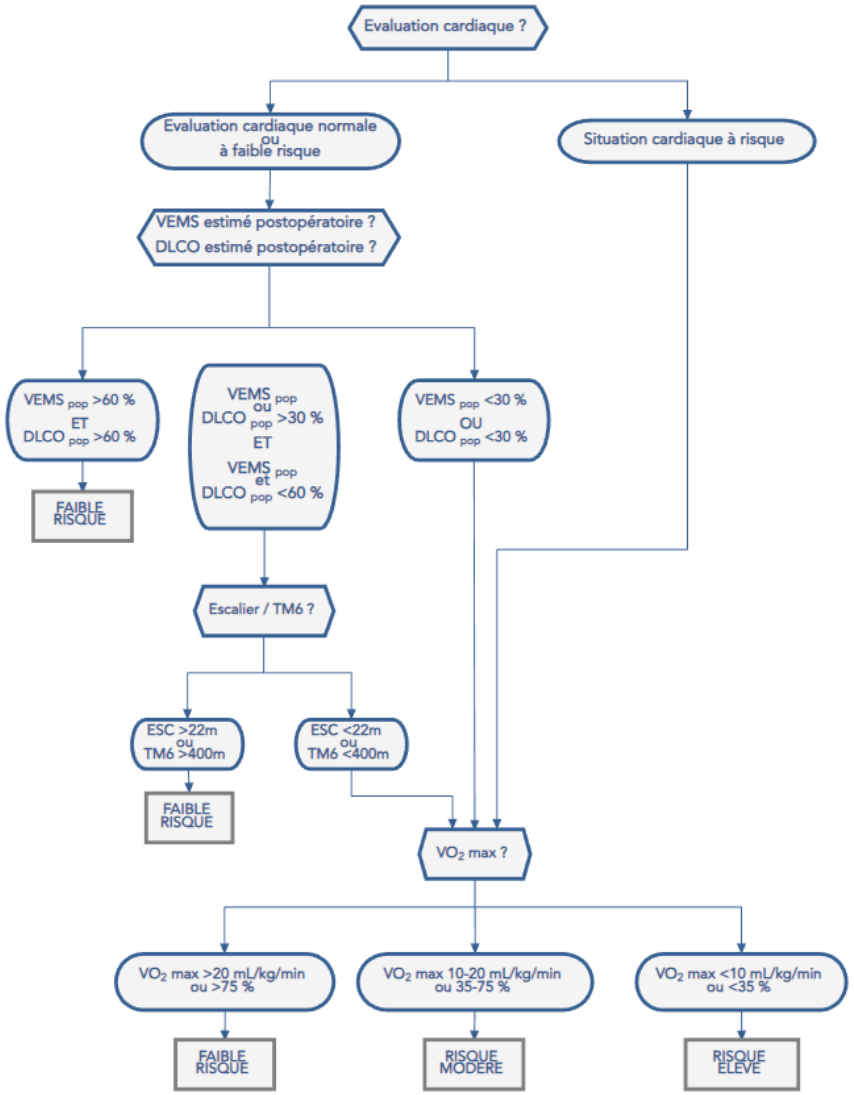


Si cardiopathie,
Optimiser le traitement cardiologique
Ne pas arrêter un anti aggrégant d'indication coronaire +++

Recommandations



ERS / ESTS 2009



ACCP 2013

Perspectives

- Préhabilitation respiratoire
  - Ambulatoire
  - En SSR
  - Activité physique adaptée
  - À distance

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Quel geste est raisonnable?

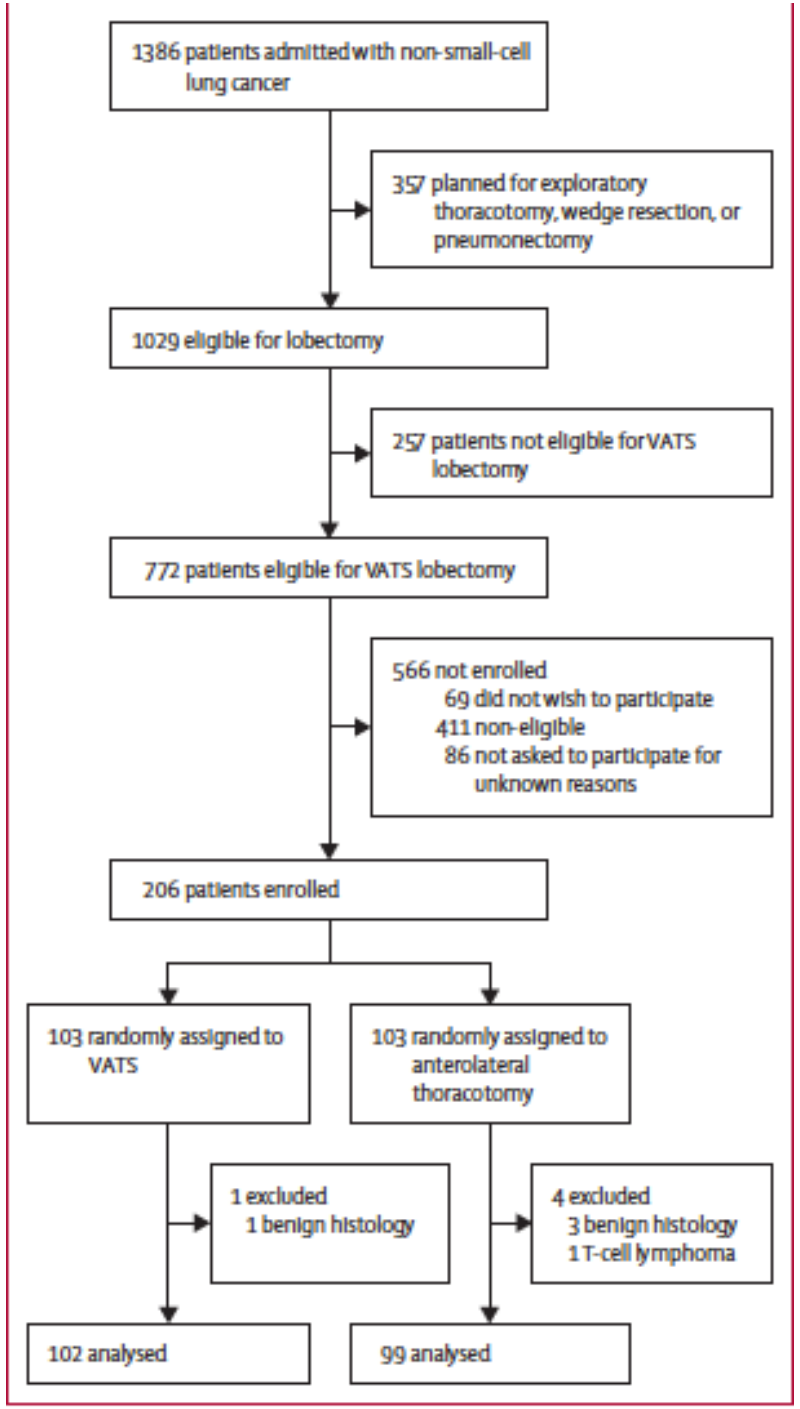
Tumeur	Ganglions	Métastases	Terrain
T1-T2-T3 accessibles à une lobectomie	N0 N1	M0	Age<80 Fct respi n Fct cardio n
Pneumonectomie T3-T4 avec résection élargie: À la paroi Aux vaisseaux Au cœur Au rachis…	N2	Métastase unique Cérébrale Surrénalienne Cancers multiples	Age>80 Fct respi limite Fct cardio limite
Pneumonectomie élargie	N3	Métastases multiples Ou os, foie, autre	Insuff respi Insuff cardio Coronaire instable

Quelle voie d'abord ? VATS

Video-assisted thoracoscopic surgery (VATS) lobectomy using a standardized anterior approach

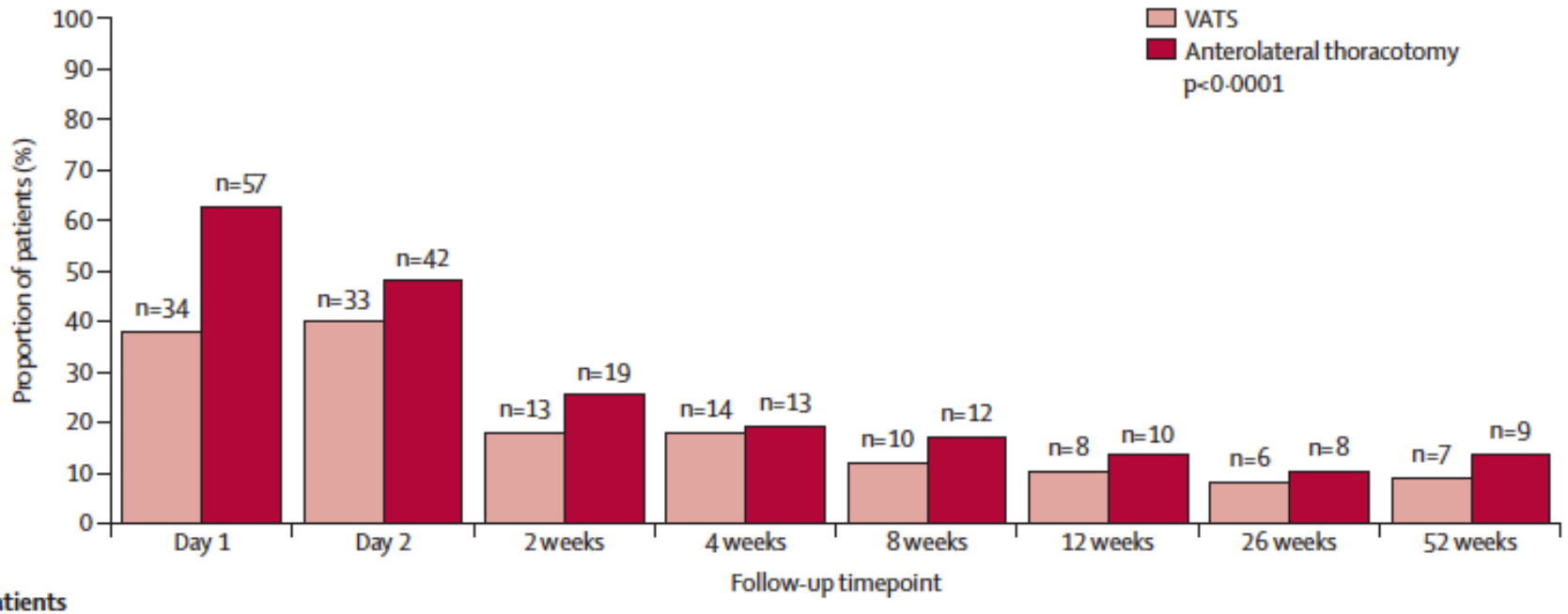
Henrik Jessen Hansen · René Horsleben Petersen · Merete Christensen

Hansen Surg Endosc 2011



Bendixen Lancet Oncol 2016

Chirurgie vidéo-assistée

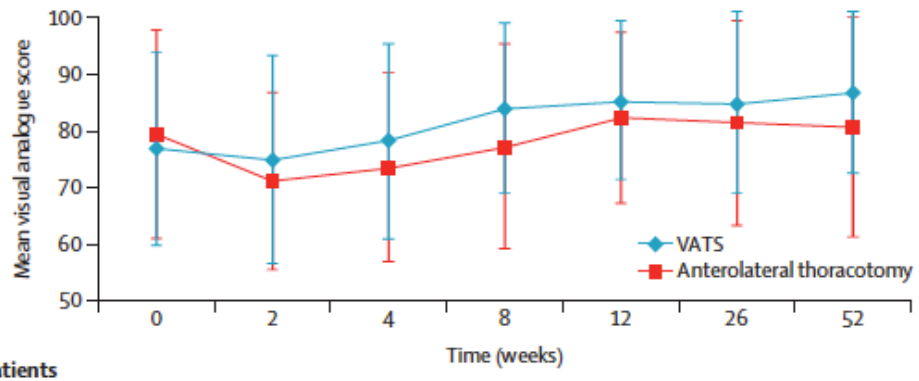


Number of patients with data available	Day 1	Day 2	2 weeks	4 weeks	8 weeks	12 weeks	26 weeks	52 weeks
VATS	89	83	74	79	83	84	80	76
Anterolateral thoractomy	90	89	76	68	72	75	74	66

Nombre de patients ayant une EVA > ou = à 3

Bendixen Lancet Oncol 2016

Chirurgie vidéo-assistée



Number of patients with data available							
VATS	59	61	63	70	75	73	73
Thoracotomy	59	65	62	62	63	67	65

Figure 3: **Self-reported quality of life by the EQ5D questionnaire**

	VATS	Anterolateral thoracotomy	p value
Preoperative	76·8 (17·1)	79·3 (18·3)	0·31
2 weeks	74·9 (18·3)	71·1 (15·6)	0·077
4 weeks	78·1 (17·2)	73·5 (16·6)	0·053
8 weeks	83·9 (15·4)	77·2 (18·1)	0·017
12 weeks	85·3 (14·3)	82·2 (14·7)	0·14
26 weeks	84·9 (16·2)	81·3 (17·5)	0·18
52 weeks	86·7 (14·2)	80·6 (19·3)	0·012

Data are mean (SD) unless otherwise stated. p values are for comparisons of means by Student's *t* test for parametric means. VATS=video-assisted thoracoscopic surgery. EQ5D= EuroQol 5 Dimensions.

Table 2: **Self-reported quality-of-life score from the EQ5D questionnaire by timepoint**

Bendixen Lancet Oncol 2016

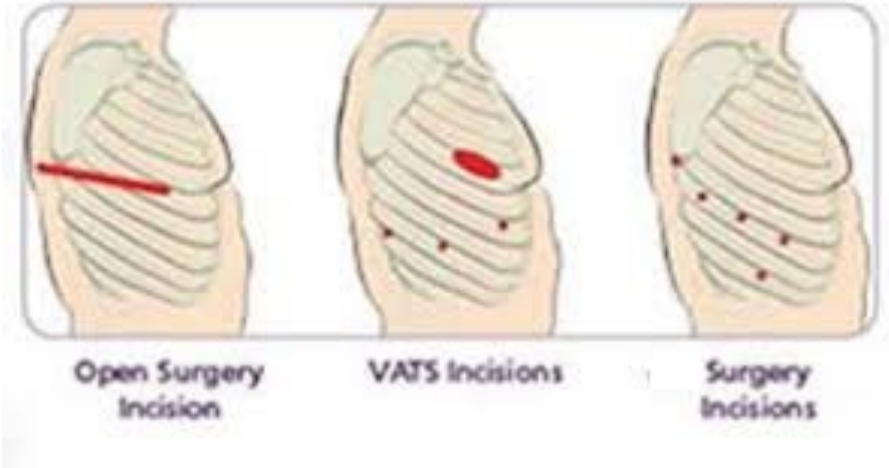
Chirurgie vidéo-assistée

- Voie d'abord de référence
  pour les lobectomies des stades I cliniques

- Intérêt
  - sur les douleurs
  - chez les patients fragiles
  - chez les patients âgés

- Limites
  - Instruments longs et non articulés
  - Vision 2D
  - Curage ganglionnaire => stades II ?
  - Segmentectomies complexes (S6 OK, S3 difficile…)

Quelle voie d’abord ? Chirurgie robot-assistée



Chirurgie robot-assistée

Chirurgie robot-assistée

Peu de publications prospectives

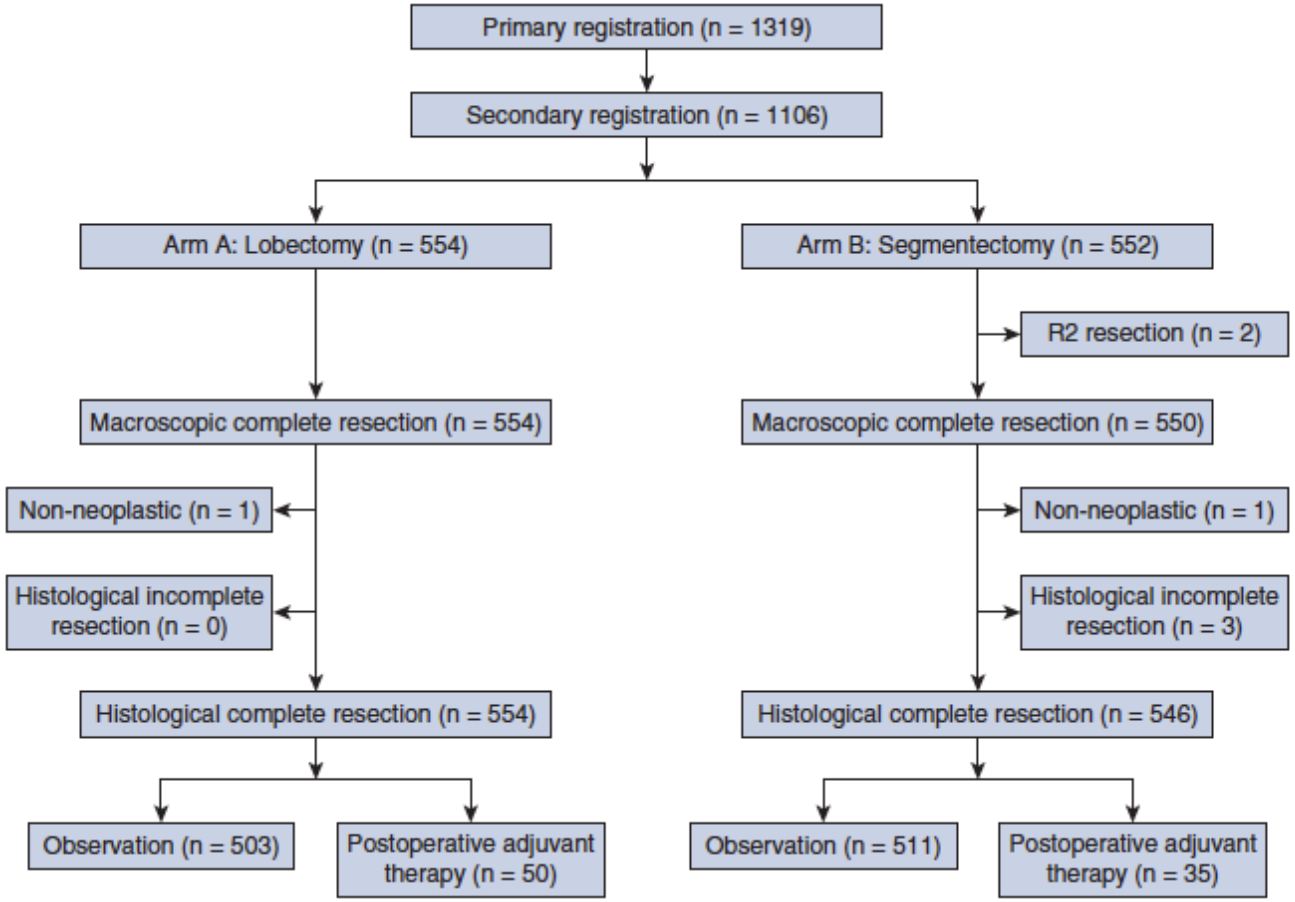
- court terme surtout = rassurantes
- long terme = rassurantes

Probablement pas mieux que la vidéo pour une lobectomie simple

Intérêt technique

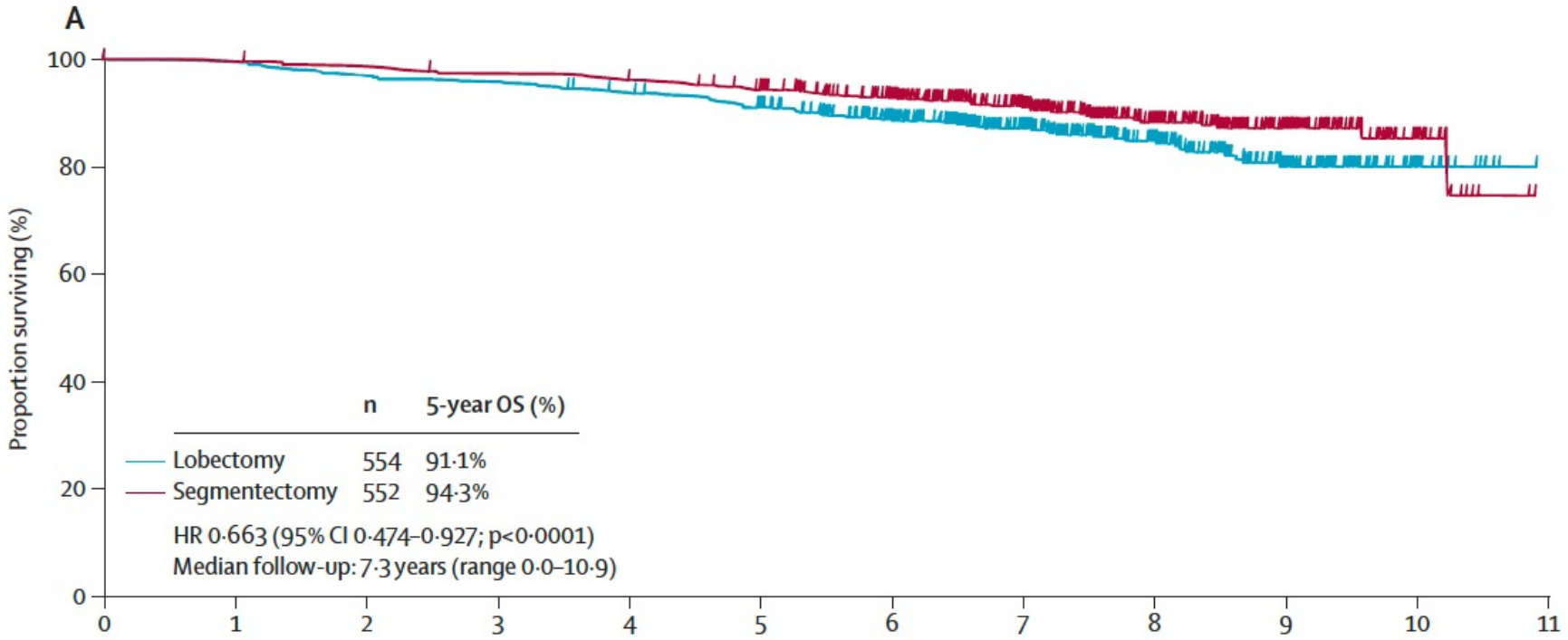
- Curage ganglionnaire => N1? N2 post induction ?
- Segmentectomies +++

JCOG0802 : results



Suzuki K *JTCS* 2019, Saji *Lancet* 2022

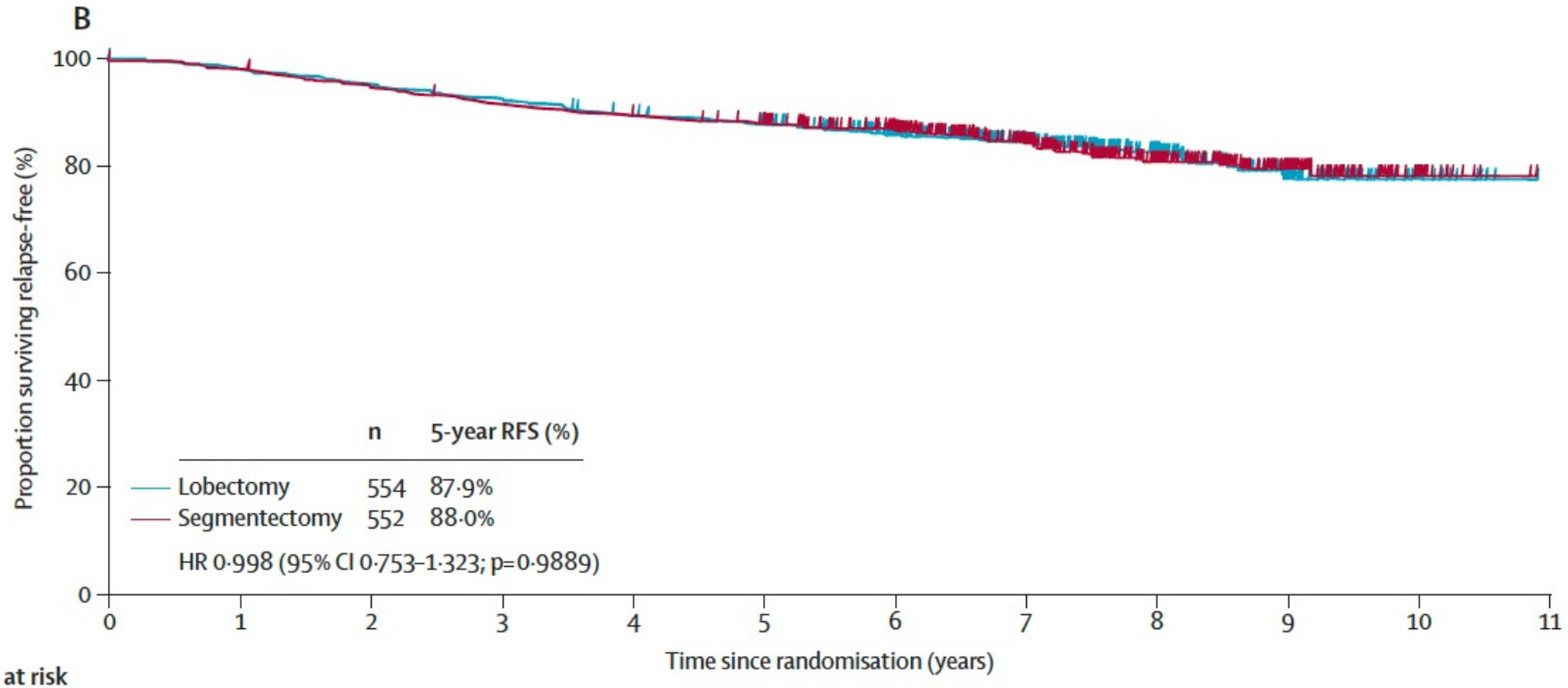
JCOG0802 : primary outcome



Number at risk (number censored)												
Lobectomy	554 (0)	550 (1)	537 (0)	530 (0)	525 (3)	495 (6)	426 (57)	322 (97)	190 (125)	90 (92)	23 (67)	0 (23)
Segmentectomy	552 (0)	549 (1)	543 (1)	534 (1)	528 (0)	512 (6)	457 (47)	332 (118)	202 (122)	104 (96)	25 (78)	0 (24)

Saji Lancet 2022

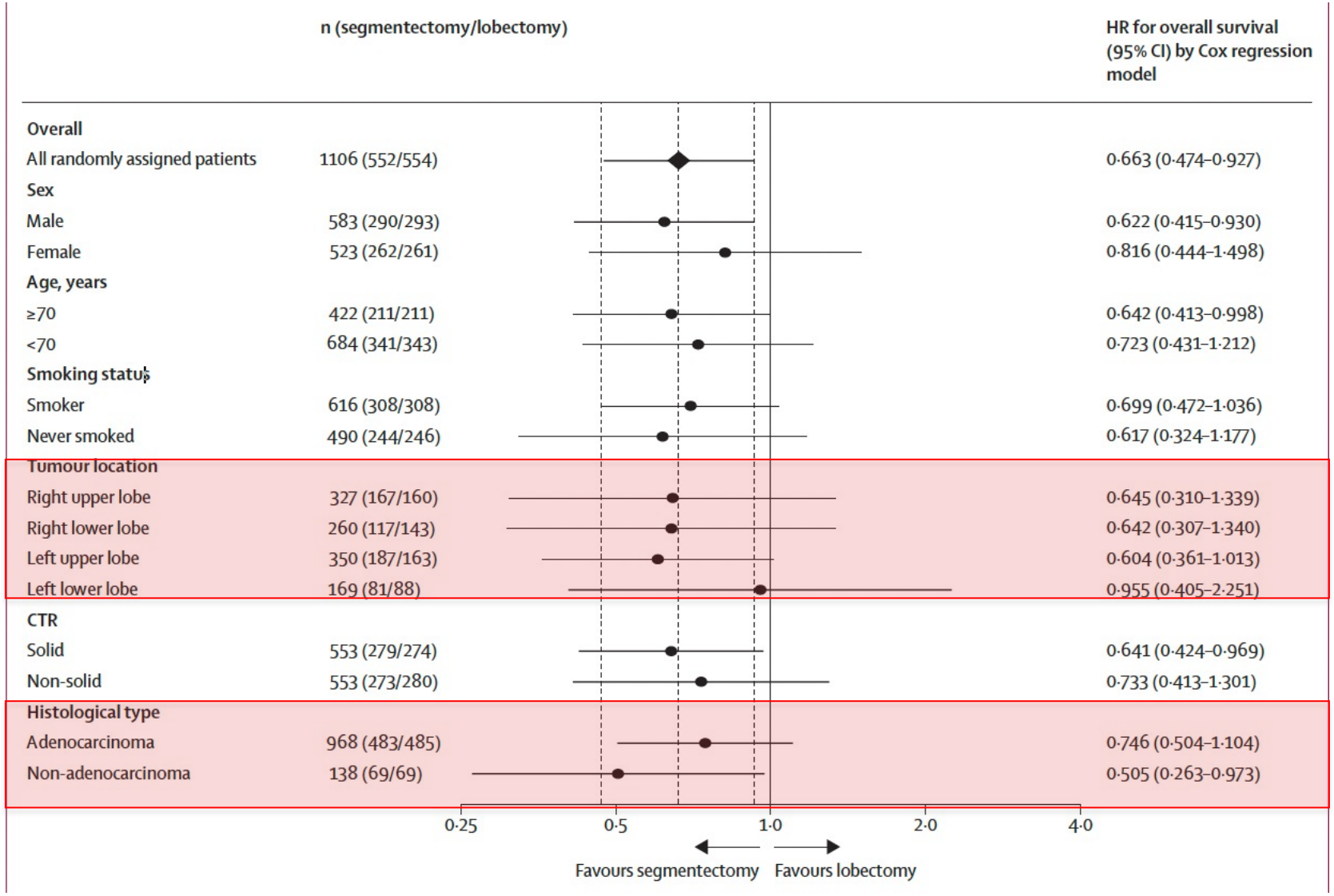
JCOG0802 : DFS



Number at risk (number censored)												
Lobectomy	554 (0)	542 (1)	527 (0)	512 (0)	492 (3)	477 (6)	409 (57)	310 (93)	184 (121)	85 (91)	22 (63)	0 (22)
Segmentectomy	552 (0)	541 (1)	521 (1)	503 (1)	491 (0)	477 (6)	426 (45)	304 (112)	181 (112)	89 (90)	21 (67)	0 (21)

Saji Lancet 2022

JCOG0802 : subgroup analysis



Saji Lancet 2022

JCOG0802 : NSCLC mortality

	Lobectomy group (n=554)	Segmentectomy group (n=552)
Total deaths	83	58
Lung cancer death	28	26
Other death	52	27
Other cancer (including second primary lung cancer)	31	12
Non-malignant disease	21	15
Respiratory disease	8	4
Cerebrovascular disease	7	2
Cardiovascular disease	4	4
Other diseases	2	5
Unknown	3	5

141 patients died during the follow-up period. *At median follow-up of 7·3 years (range 0·0–10·9).

Table 2: **Summary of causes of death during follow-up***

<u>Récidives locales</u>
segment n=58, 11%
lobectomy n=30, 5%
p=0·0018

Saji Lancet 2022

Buts de la présentation

1. Bases oncologiques de la chirurgie
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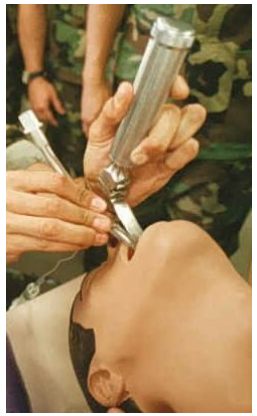
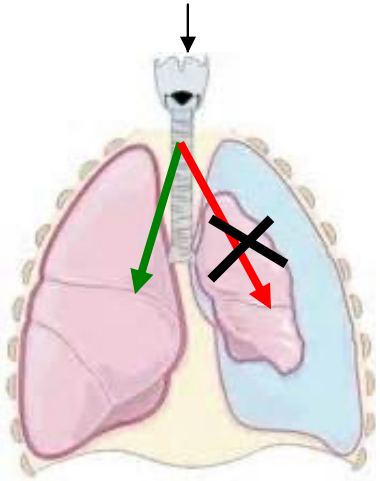
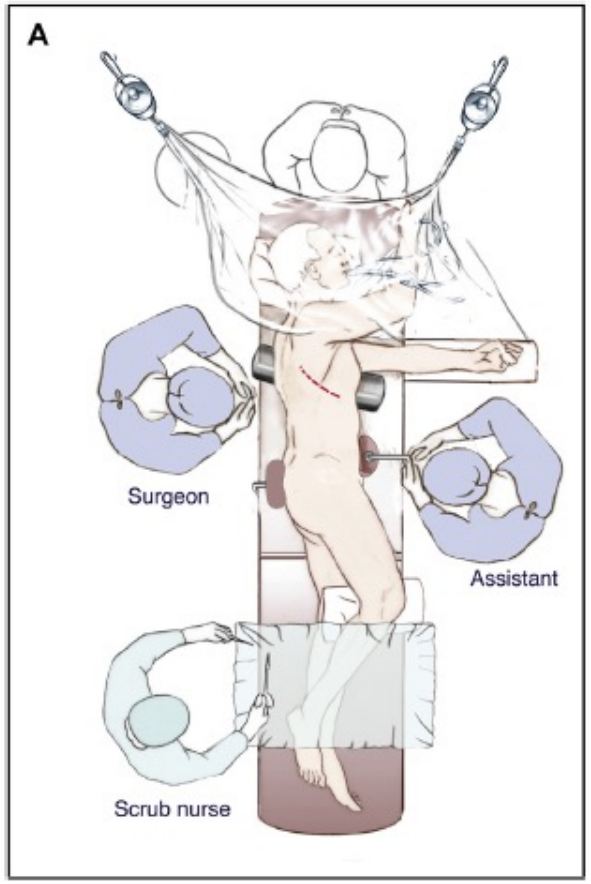
L’intervention…

- Induction - intubation sélective
- Analgésie spécifique



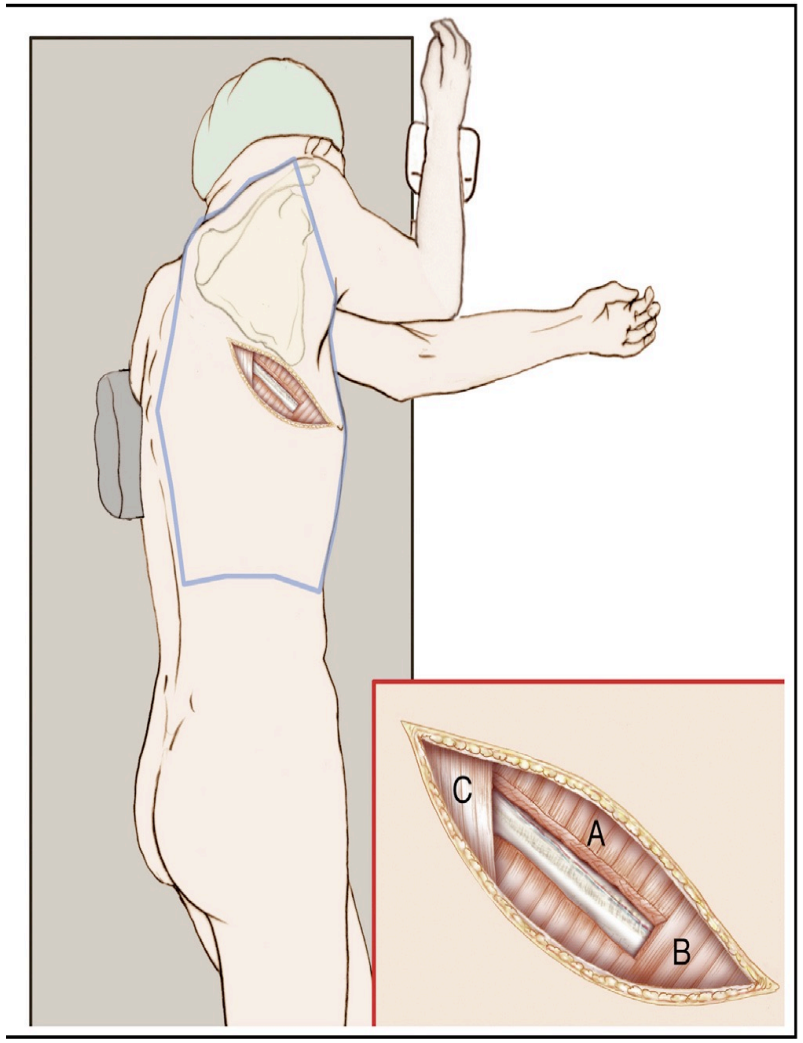


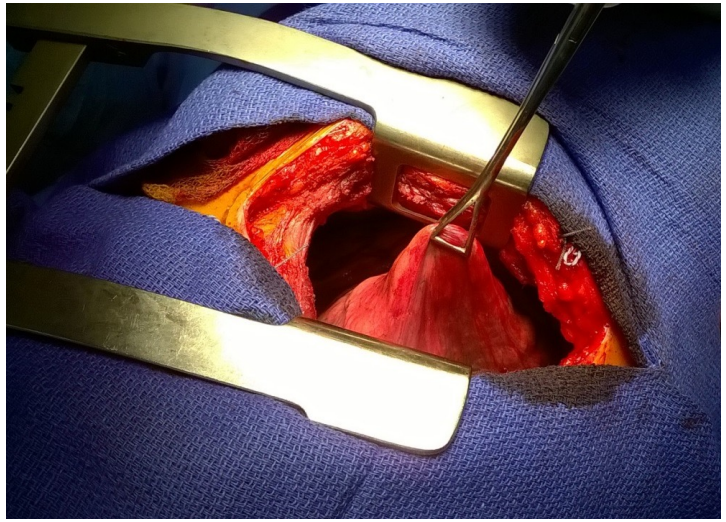
- Installation - préparation cutanée – champage



- Check list - Incision

Chirurgie ouverte





Pros

- Eye: 3D vision
- Hand: 7 degrees of freedom
- Dexterity for vessels ligation
- Dexterity for duct suturing
- Dexterity for nodes dissection

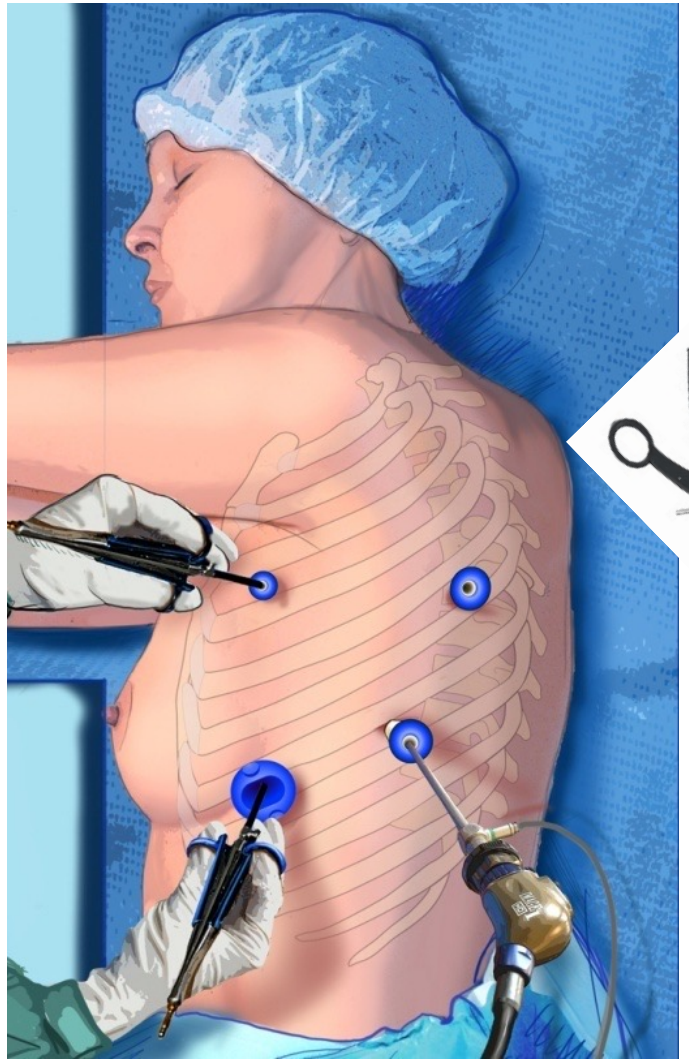
= Complex procedures possible

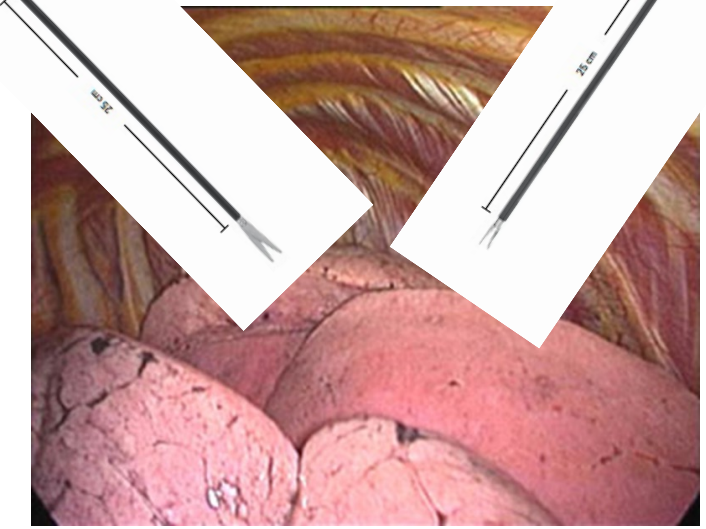
Cons

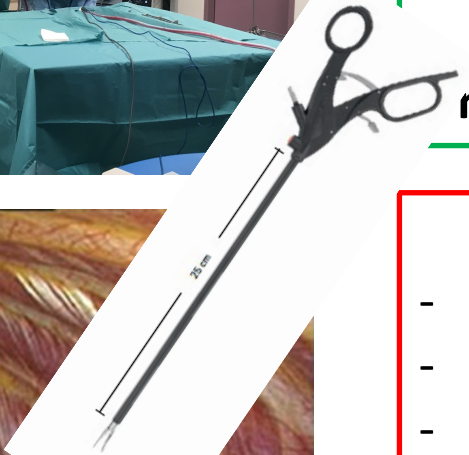
- Inflammation
- Hypothermia
- Bleeding
- Pain
- Infection

= Postoperative complications

Chirurgie vidéo - assistée







Pros

- Enhanced vision
- Less inflammation
- Less hypothermia
- Less bleeding
- Less pain

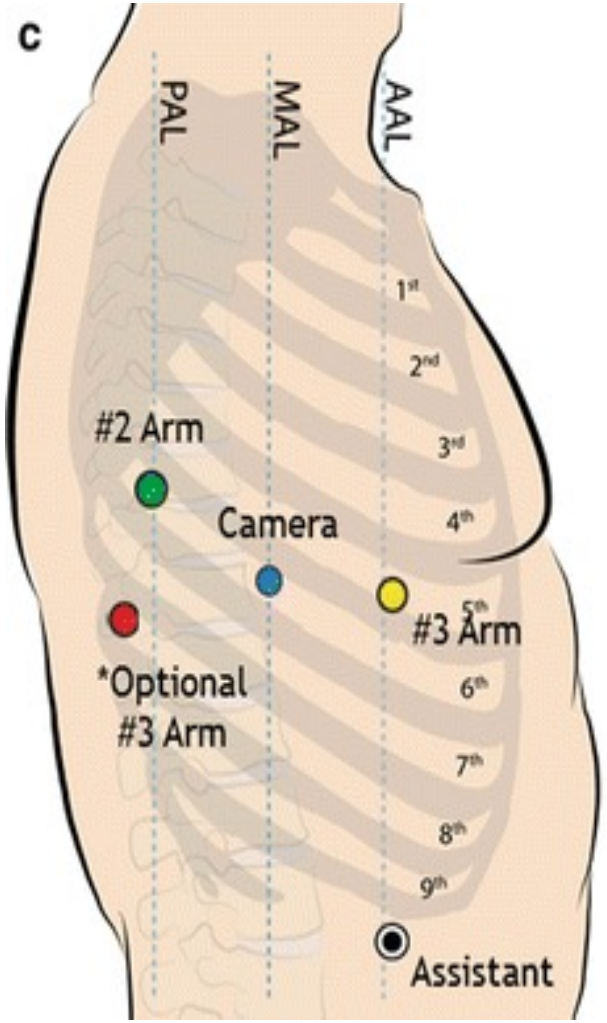
minimally invasive surgery

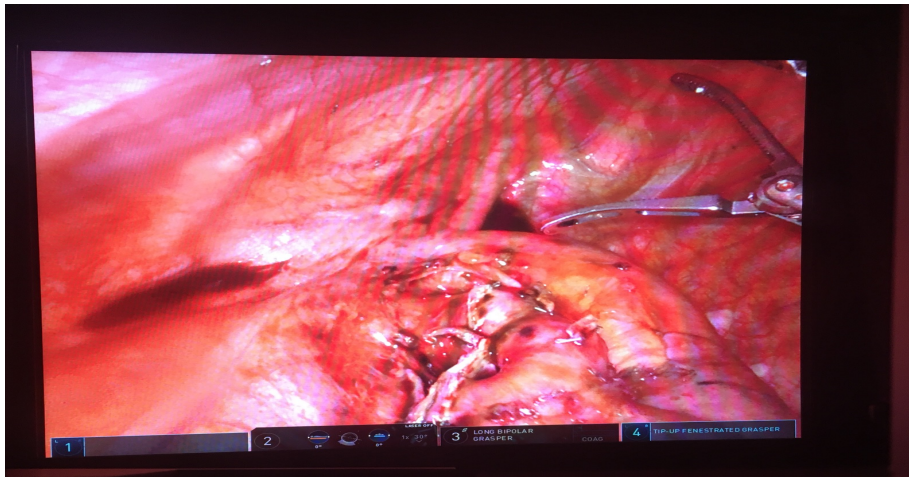
Cons

- 2D vision => 3D ?
- Fulcrum effect
- Straight instruments
- Difficult to ligate a vessel
- Difficult to suture a duct
- Difficult to dissect a node

= limited to simple procedures

Chirurgie robot-assistée





Pros

- **minimally invasive surgery**
- 3D vision
- No fulcrum effect
- Wristed extremities
- Possible to ligate a vessel
- Possible to suture a duct
- Possible to dissect a node

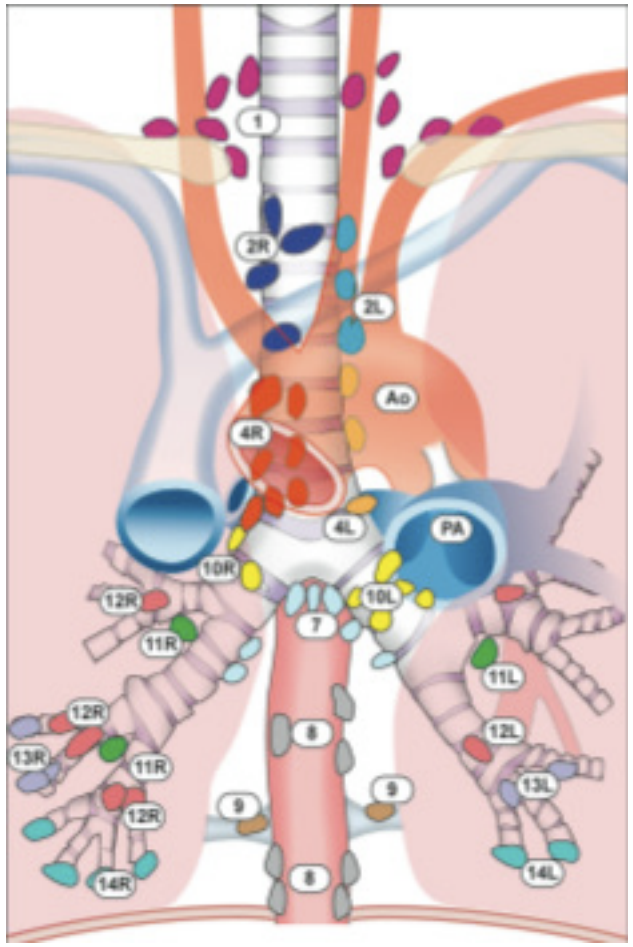
= allow complex procedures

Cons

- Changes of habits
- Changes of workflow
- Straight instruments
- No tactile feedback
- Price

= limited success initially in Fr.

2R
4R
10R
11
11
7
8R
DERMOTRACE®


1
2R
2L
Ao
4R
4L
PA
10R
10L
7
12R
11R
11L
12R
13R
11R
12L
13L
12R
9
9
14R
8
8
14L

Récupération Améliorée après Chirurgie

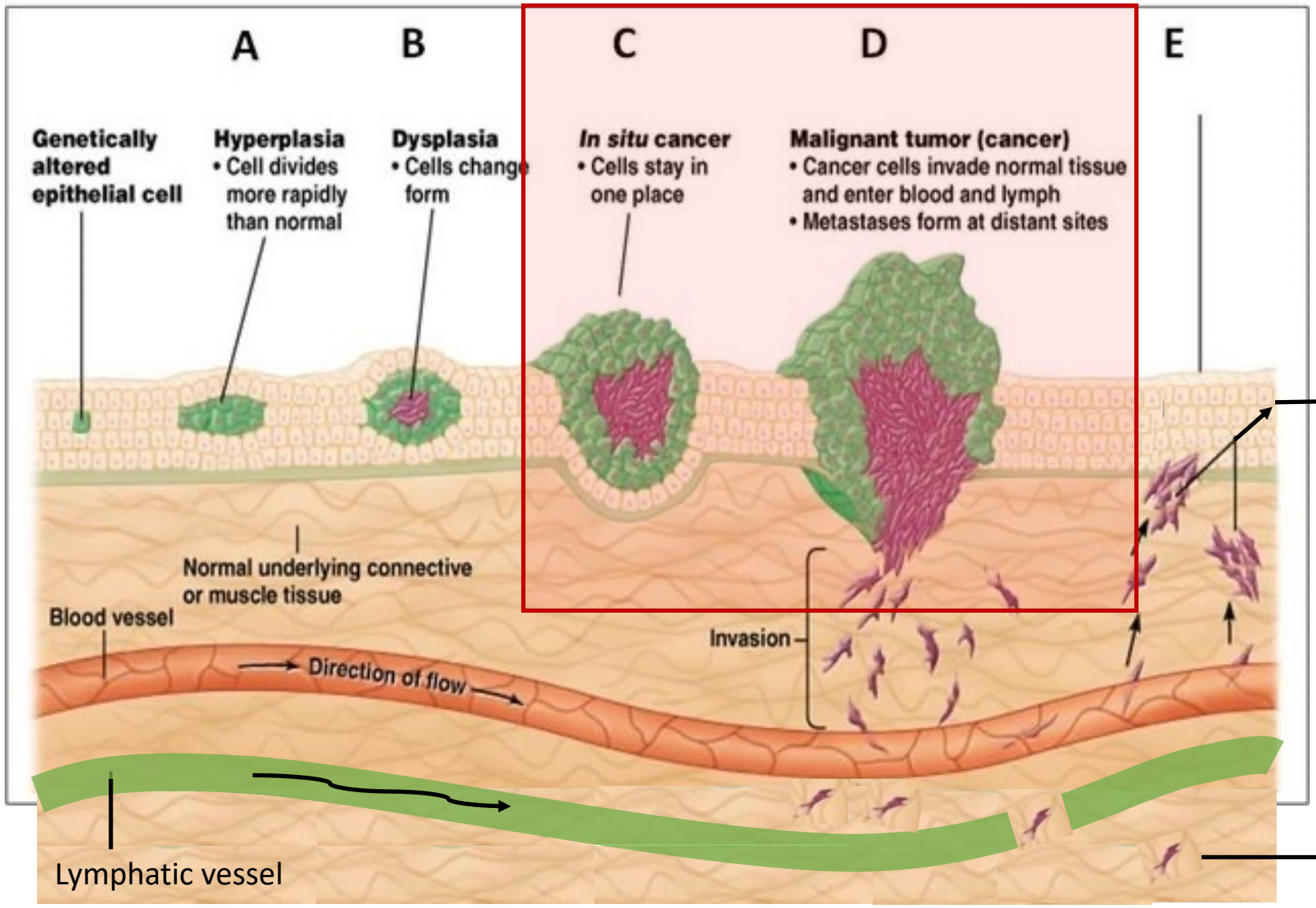
- Diminuer le stress de l'intervention et s'adapter aux capacités de récupération du patient
  - J0 6h: Café, thé, jus de fruit sans pulpe
  - J0 8h: bloc pour AG
  - J0 9h-11h: intervention
  - J0 11h-16h: salle de réveil avec kiné+++
  - J0 17h : retour avec mobilisation et diner au fauteuil
  - J1: Ablation VVP, ablation 1er drain, marche
  - => sortie à partir de J2 pour les abords vidéo ou robot assistés
  - J2: Ablation KT ALR, ablation 2ème drain, marche
  - => sortie à partir de J3 pour les abords ouverts

Complications

- Les plus fréquentes:
  - Encombrement bronchique => pneumopathies
  - Fuites aériennes prolongées => drainage prolongé
  - Troubles du rythme: FA paroxystique => réduction ou ralentissement

- Chiffres nationaux après lobectomie:
  - Mortalité J90 = 1-3%
  - Morbidité grade 3-4 J90 = 10-20%
  - DMS 6 jours

Progression tumorale



Metastases

Lymph nodes

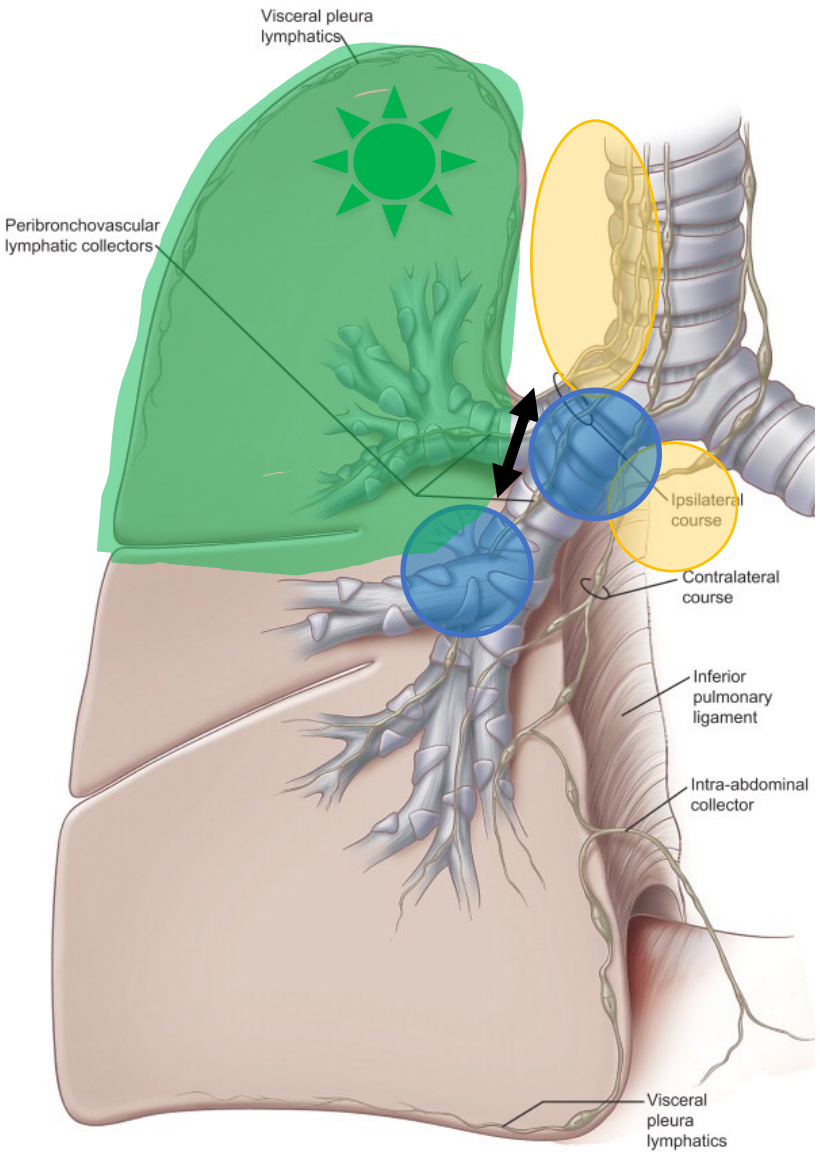
Bases de la chirurgie oncologique

Complete resection
- Tumor
- Anatomical segment
- Vessels + bronchus
- Adequate margins

Lymph node management
- SLN Dissection

Low rate of complications

Multimodal treatment
- Chemotherapy
- Immunotherapy
- Targeted therapy
- Radiation therapy



Buts de la présentation

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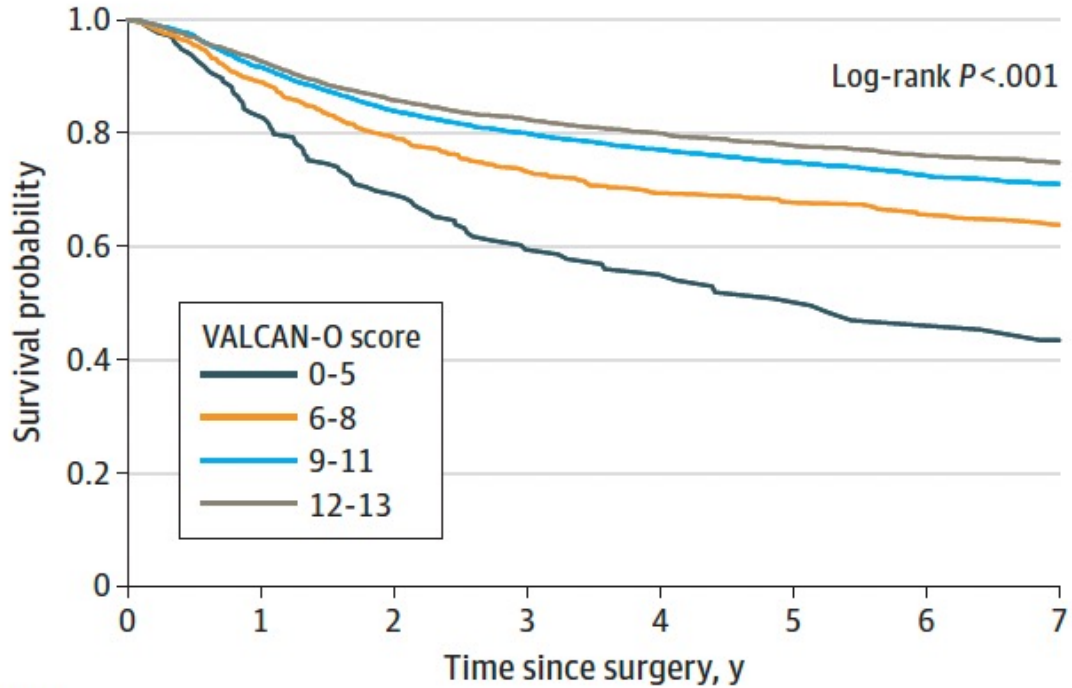
B Recurrence-free survival



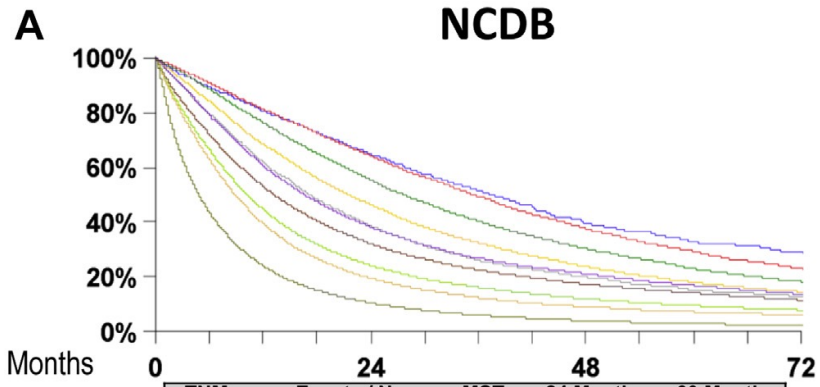
No. at risk								
0-5	231	149	112	74	56	44	30	0
6-8	983	766	608	504	389	290	213	0
9-11	5030	4180	3540	3096	2627	2088	1635	0
12-13	3343	2875	2494	2220	1857	1381	1026	0

Pathologic stage	
I	8385 (87.1)
II	794 (8.2)
III	408 (4.2)
IV	41 (0.4)

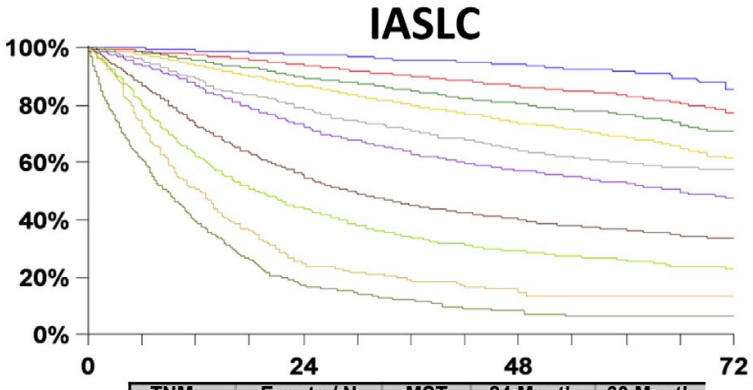
Heiden et al, JAMA Surg 2023

OS, cTNM

A



cTNM	Events / N	MST	24 Month	60 Month
IA1	792 / 1441	37.5	65%	33%
IA2	6288 / 10698	35.6	64%	29%
IA3	7171 / 10941	27.9	55%	23%
IB	7780 / 10575	21.6	46%	18%
IIA	3608 / 4787	17.3	39%	15%
IIB	12814 / 16833	16.7	38%	17%
IIIA	62359 / 75778	13.3	32%	14%
IIIB	62800 / 72372	10.2	24%	10%
IIIC	16255 / 18189	8.9	20%	7%
IV	364782 / 390920	4.8	11%	3%



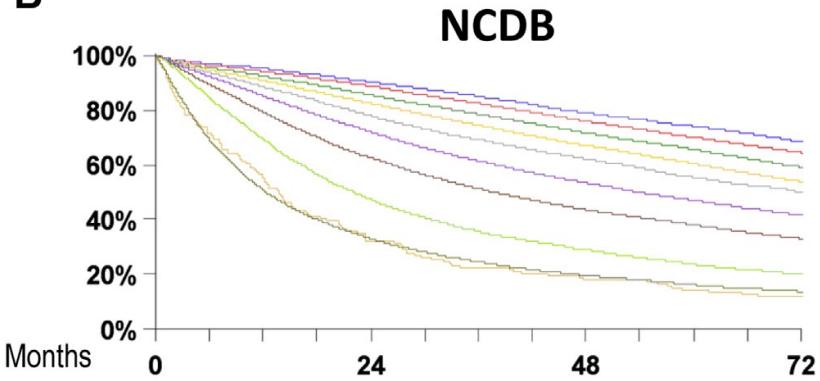
cTNM	Events / N	MST	24 Month	60 Month
IA1	68 / 781	NR	97%	92%
IA2	505 / 3105	NR	94%	83%
IA3	546 / 2417	NR	90%	77%
IB	560 / 1928	NR	87%	68%
IIA	215 / 585	NR	79%	60%
IIB	605 / 1453	66.0	72%	53%
IIIA	2052 / 3200	29.3	55%	36%
IIIB	1551 / 2140	19.0	44%	26%
IIIC	831 / 986	12.6	24%	13%
IV	664 / 882	8.8	17%	6%

5% chirurgie

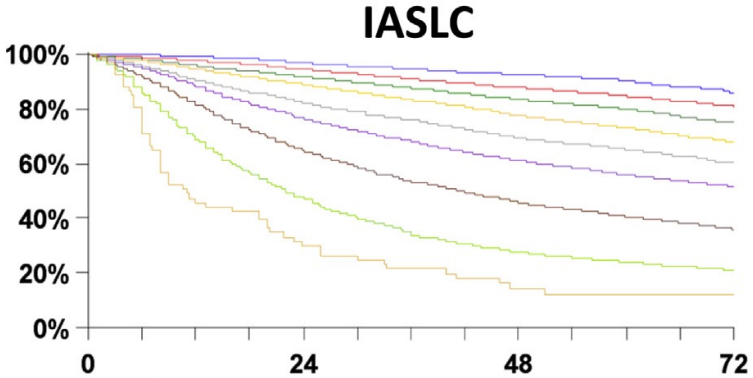
85% chirurgie

OS, pTNM

B



pTNM	Events / N	MST	24 Month	60 Month
IA1	1896 / 7133	117.6	90%	74%
IA2	10135 / 33196	101.9	89%	70%
IA3	8464 / 23627	89.5	86%	66%
IB	11795 / 29355	80.1	82%	60%
IIA	3617 / 8127	72.4	78%	55%
IIB	14959 / 29171	54.0	72%	47%
IIIA	18555 / 29711	37.8	63%	38%
IIIB	4190 / 5626	22.2	47%	24%
IIIC	150 / 178	13.8	33%	15%
IV	13656 / 16492	12.4	33%	16%



pTNM	Events / N	MST	24 Month	60 Month
IA1	139 / 1389	NR	97%	90%
IA2	823 / 5633	NR	94%	85%
IA3	875 / 4401	NR	92%	80%
IB	1618 / 6095	NR	89%	73%
IIA	556 / 1638	NR	82%	65%
IIB	2175 / 5226	NR	76%	56%
IIIA	3219 / 5756	41.9	65%	41%
IIIB	1215 / 1729	22.0	47%	24%
IIIC	55 / 69	11.0	30%	12%

Chansky JTO 2017

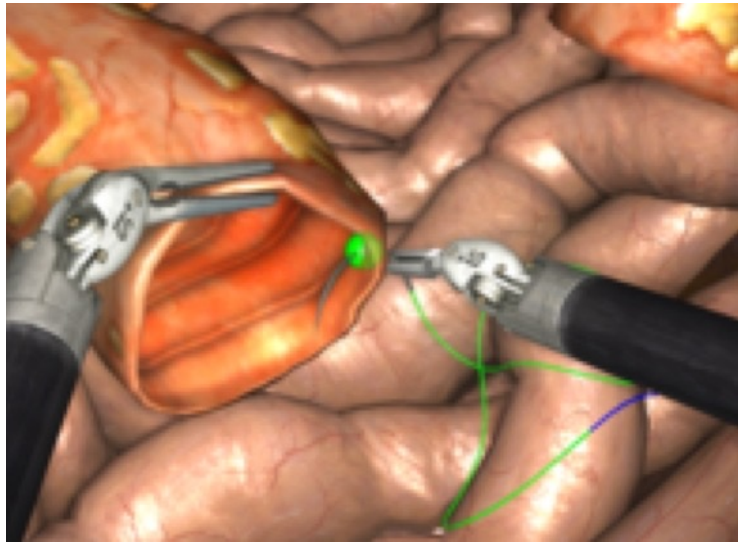
Table 2. Adverse Events.*

Event	Nivolumab plus Chemotherapy (N=176)		Chemotherapy Alone (N=176)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Adverse events of any cause — no. (%)†				
All	163 (92.6)	72 (40.9)	171 (97.2)	77 (43.8)
Leading to discontinuation of treatment	18 (10.2)	10 (5.7)	20 (11.4)	7 (4.0)
Serious	30 (17.0)	19 (10.8)	24 (13.6)	17 (9.7)
Treatment-related adverse events — no. (%)†				
All	145 (82.4)	59 (33.5)	156 (88.6)	65 (36.9)
Leading to discontinuation of treatment	18 (10.2)	10 (5.7)	17 (9.7)	6 (3.4)
Serious	21 (11.9)	15 (8.5)	18 (10.2)	14 (8.0)
Death‡	0	—	3 (1.7)	—
Surgery-related adverse events — no./total no. (%)§	62/149 (41.6)	17/149 (11.4)	63/135 (46.7)	20/135 (14.8)

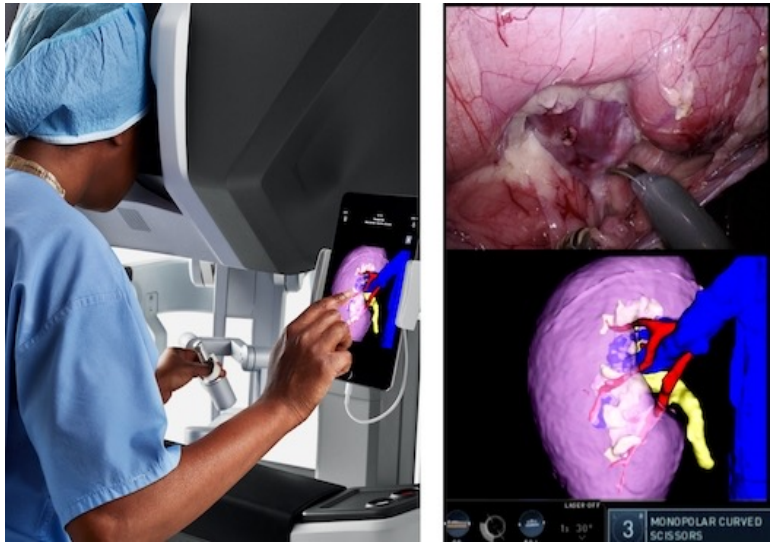
Checkmate 816 Forde NEJM 2022

Perspectives

Training



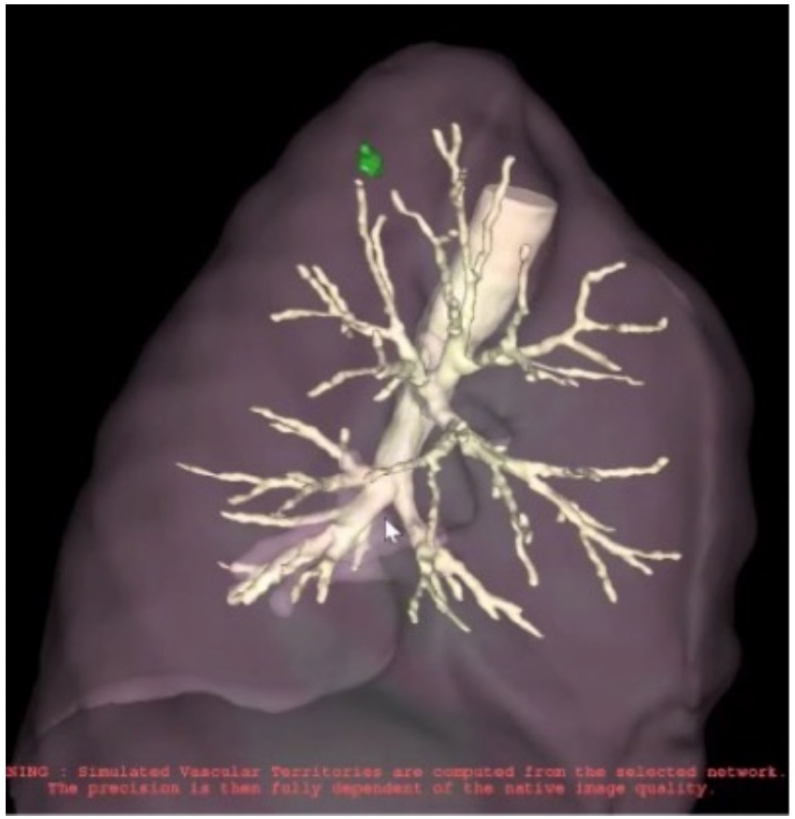
Imaging

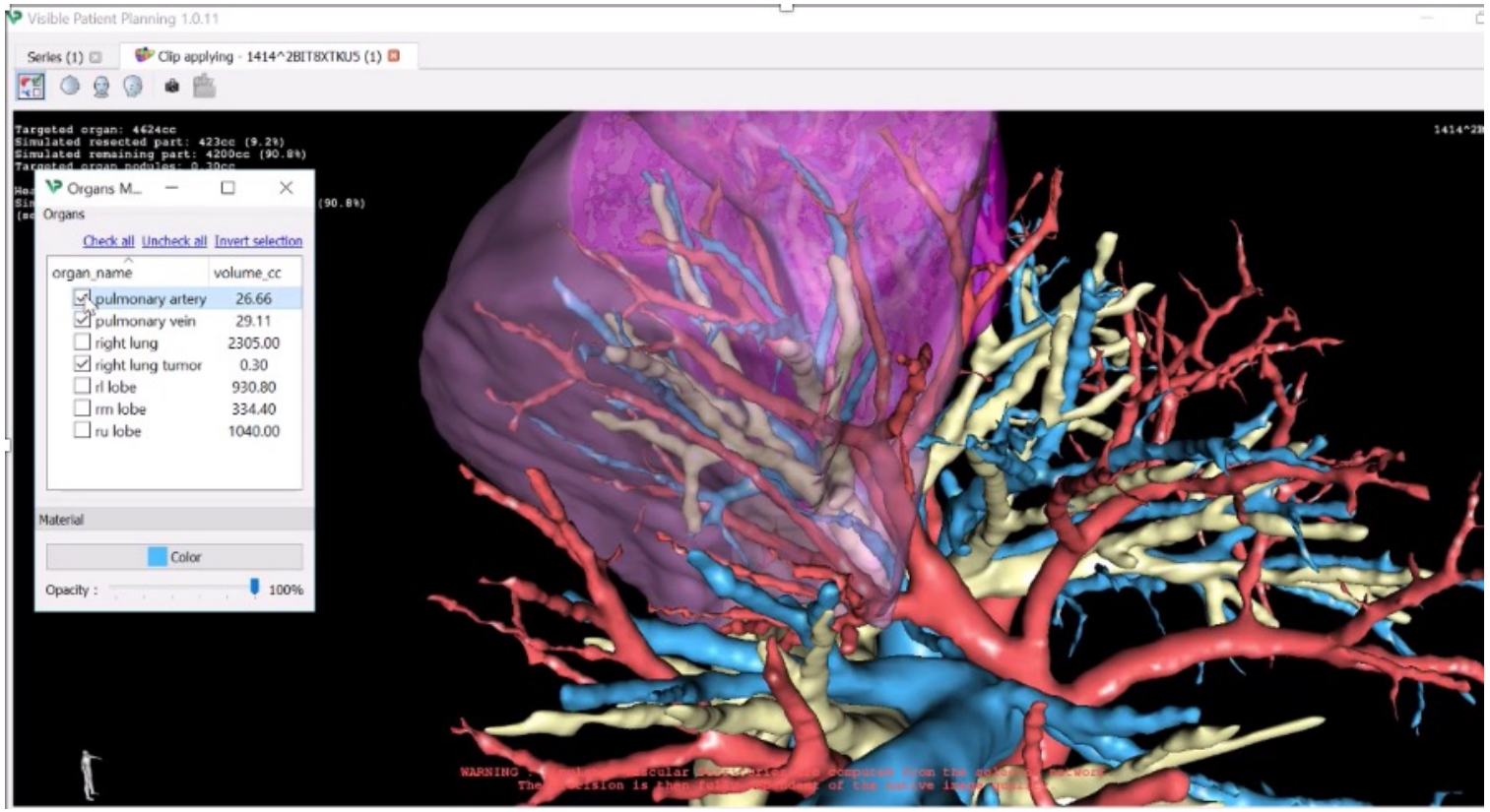


Data and analytics

Single port system

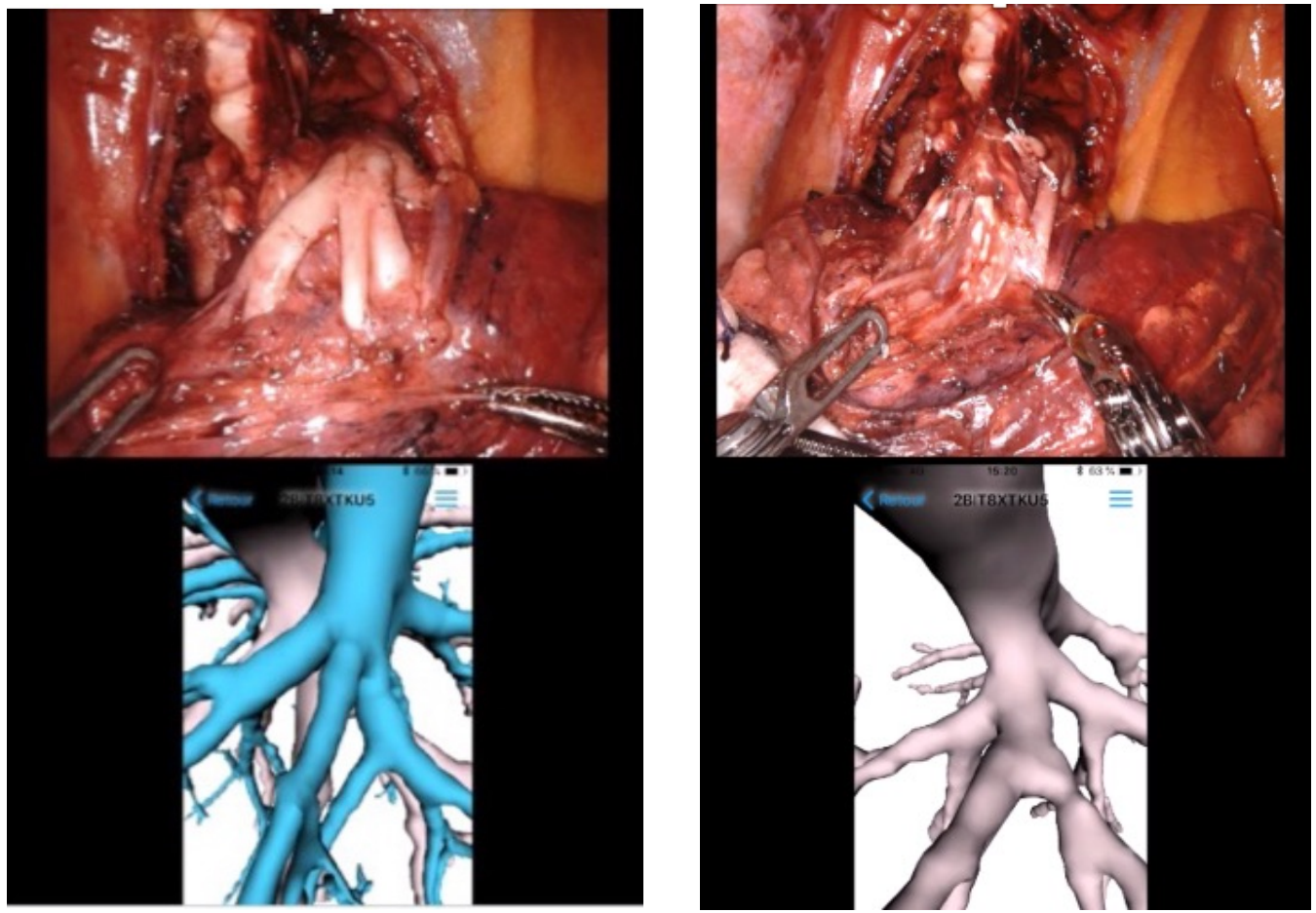
Perspectives: software





From 3D reconstruction to planification

Perspectives: software



From 3D reconstruction to planification and then superimposition ?

Perspectives: microscopic residual disease

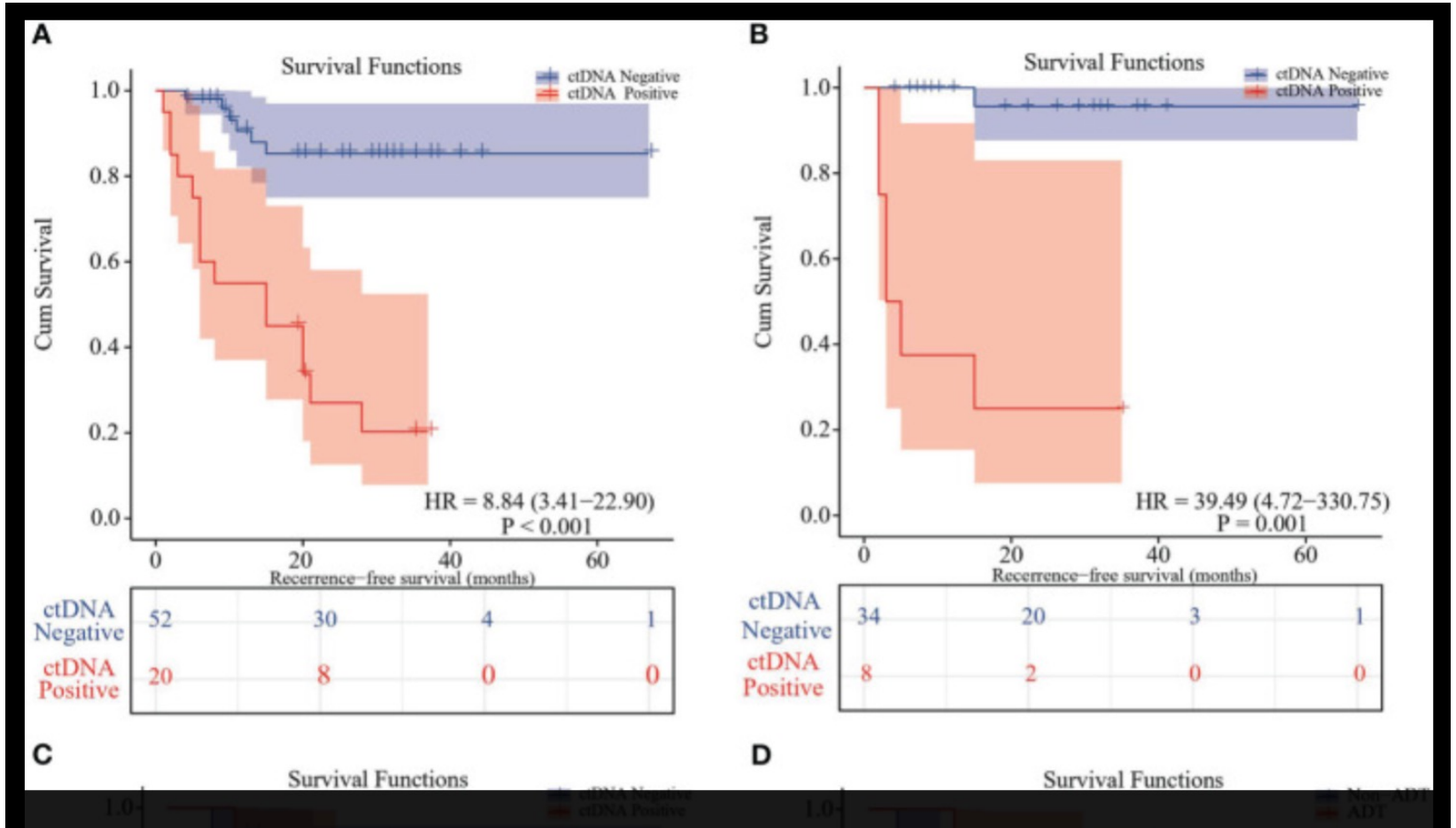


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Figure 1 Kaplan–Meier curve in patients stratified by postsurgical ctDNA status. **(A)**

Zhang Front Oncol 2023

Conclusion

- Les stades localisés opérables comprennent des situations très variées
- L'intervention de lobectomie / curage est associée à de bons résultats chirurgicaux (taux de complications) et oncologiques (R0, upstaging N)
- Stade II: tendance à l'escalade
  - Ajout de l'immunothérapie à la séquence chirurgie - chimiothérapie
- Stade I: tendance à la désescalade
  - Abord par VATS ou RATS > ouvert
  - Tumeurs de 2 à 4 cm ou localisation centrale : lobectomie / curage
  - Tumeurs de moins de 2 cm, périphérique, solide: segmentectomie / curage
  - Tumeurs de moins de 2 cm, périphérique, GGO : wedge ? Essai en cours