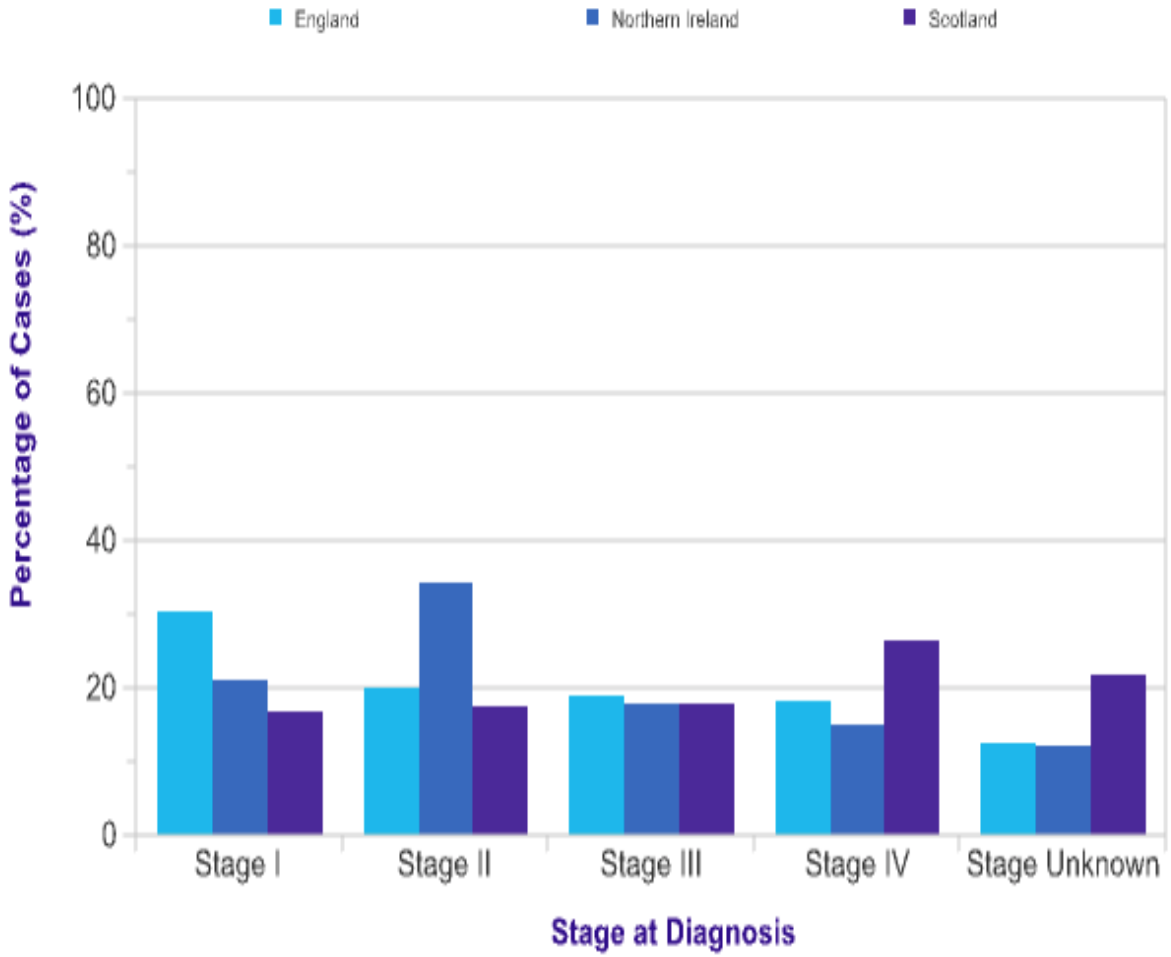
Prostate Cancer Management

Mr Matt Simms
Consultant Urological Surgeon
Hull and East Yorkshire Hospitals NHS Trust

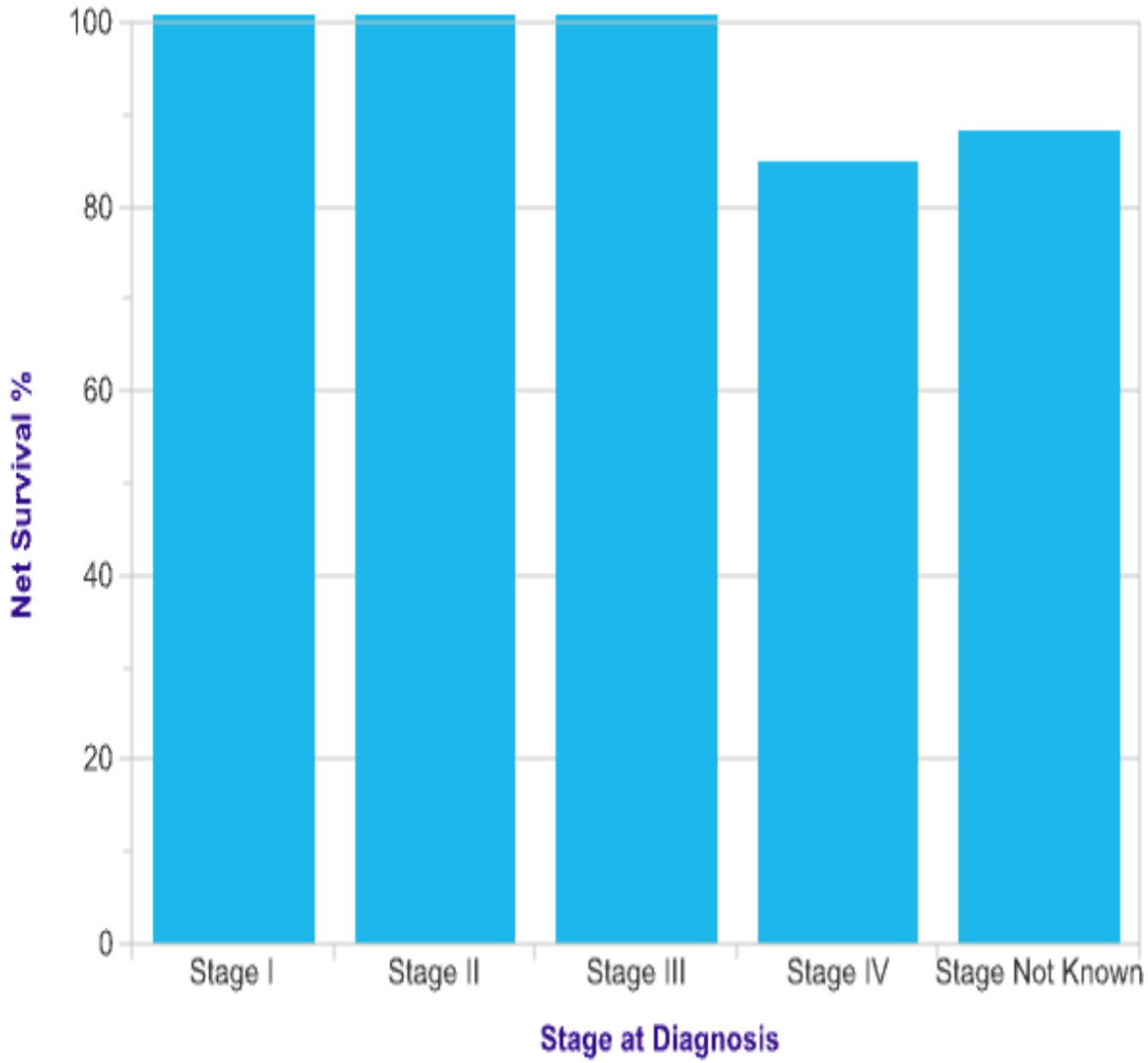
Management Depends on Stage And Prediction of Natural History

- Localised
- Locally Adavanced
- Metastatic

Prostate Cancer (C61), Proportion of Cases Diagnosed at Each Stage, All Ages, England 2014, Scotland 2013-2014, Northern Ireland 2010-2014



Prostate Cancer (C61), One-Year Age Standardised Net Survival by Stage, Adults (Ages 15-99 Years), England 2014



Staging

TABLE 1: 2010 TNM staging system of prostate cancer

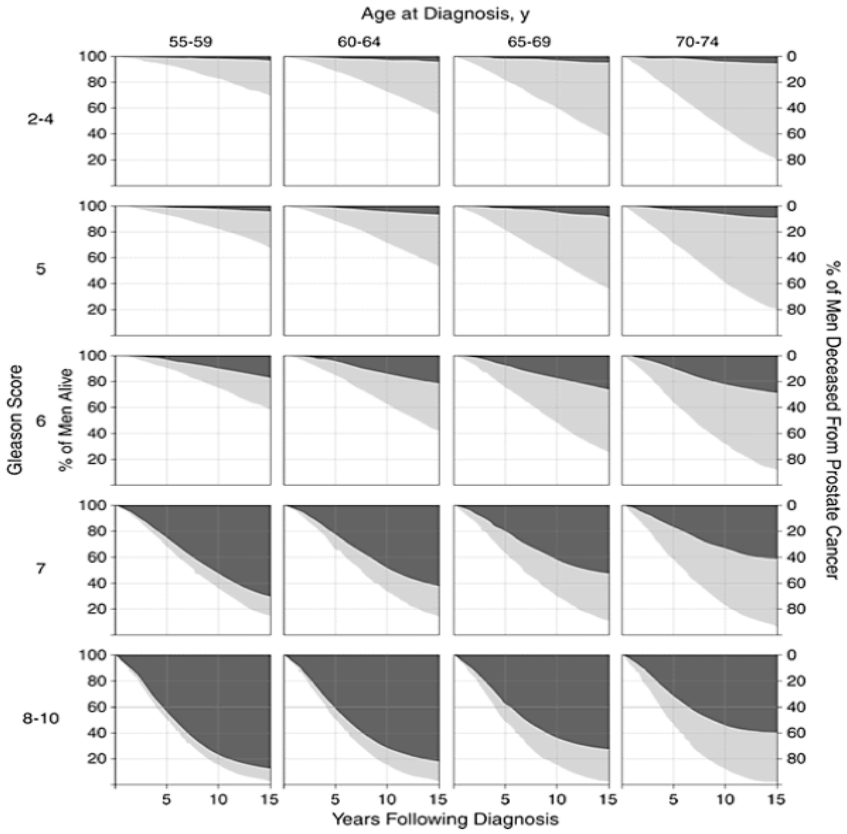
Localized disease	
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Clinically inapparent tumor neither palpable nor visible by imaging
T1a	Tumor incidental histologic finding in ≤ 5% of resected tissue
T1b	Tumor incidental histologic finding in > 5% of resected tissue
T1c	Tumor identified by needle biopsy (eg, because of elevated PSA level)
T2	Tumor confined within prostate
T2a	Tumor involves one-half of one lobe or less
T2b	Tumor involves more than one-half of one lobe but not both lobes
T2c	Tumor involves both lobes
Local extension	
T3a	Extracapsular extension (unilateral or bilateral)
T3b	Tumor invades seminal vesicle(s)
T4	Bladder invasion, fixed to pelvic side wall, or invasion of adjacent structures
Metastatic disease	
N1	Positive regional lymph nodes
M1	Distant metastasis

From Edge SB, Byrd DR, Compton CC, et al (eds): AJCC Cancer Staging Manual, 7th ed. New York, Springer, 2010.

Prostate Cancer Stage Groupings

Stage I	T1a, N0, M0, G1
Stage II	T1a, N0, M0, G2-4
	T1b, N0, M0, any G
	T1, N0, M0, any G
	T2, N0, M0, any G
Stage III	T3, N0, M0, any G
Stage IV	T4, N0, M0, any G
	Any T, N1, M0, any G
	Any T, any N, M1, any G

Natural History of Prostate Cancer



Localised Disease

- Active Surveillance
- Brachytherapy
- Ext Beam Radiotherapy
- Surgery
- Focal Therapy

Pivot Study

Wilt et al NEJM, 2012, 2017

- Randomised study of ww vs surgery
- No overall sig diff in disease specific mortaility
- Surgery may be associated with decreased mortality in men with intermediate risk disease
- Surgery associated with increased morbidity, decreased risk of disease progression

PROTECT study

- 1643 patients randomised between active treatment and active monitoring
- Majority of patients had low risk disease
- Cancer specific survival at 10 years similar between treatment and monitoring
- Increased risk of progression and metastatic risk in AM group but overall risks very low.

Active Surveillance-Who is it suitable for?

Diagnostic factor	Johns Hopkins	Sunnybrook	PRIAS
Clinical stage	T1c	T1c/T2	T1c/T2
PSA level	< 10 ng/ml	< 15 ng/ml	≤ 10 ng/ml
PSA density	< 0.15 ng/ml	--	< 0.2 ng/ml
Gleason score	≤ 6	≤ 6 *	≤ 6
Amount of cancer	1 or 2 positive cores; ≤ 50% cancer in any one core	As evaluated on an individual basis	1 or 2 positive cores

* A Gleason score of 3 + 4 = 7 has historically been acceptable in carefully selected patients in the Sunnybrook cohort.

Questions

- How often should men be biopsied
- How should they be biopsied
- What is the role of Mp MRI
- In the future are likely to rely on biomarkers

External Beam Radiotherapy

Typically given with hormones

Modern techniques may reduce GI Toxicity

Modern hypofractionated regimens can be given over 4 weeks (IMRT)

Newer techniques such as stereotactic beam radiotherapy and proton beam therapy are not yet established

Side effects

- Can be as due to hormones
- Transient bladder and bowel problems
- Fatigue
- Lower risk of stress incontinence than surgery
- Higher risk GI problems (around 10%)
- Erectile dysfunction worsens with time

Brachytherapy (LDR)

- Usually using I-125 seeds
- Suitable for smaller prostates (less than 50ml)
- Suitable for men with minimal LUTS
- Done as day case GA procedure
- Short term urinary toxicity common
- Less GI toxicity than ERBT

First radical perineal prostatectomy - Young 1905

First radical retropubic prostatectomy Millen 1949

Patrick Walsh – early 1980s- described anatomical nerve sparing radical retropubic prostatectomy

1999-2000 Laparoscopic Radical Prostatectomy- Abbou Creteil Paris,Guilloneau, Montsouris Paris

Early 2000s – first robotic prostatectomies reported in Europe

Evidence for surgery

For a patient with prostate cancer, if treatment for cure is necessary, is it possible? If possible, is it necessary?''

- **SPCG4 (Bill-Axelson study 2006, 2008,2014)**

- Improved disease specific survival, local progression and metastasis, local progression, overall mortality in surgery vs watchful waiting group- More pronounced in men less than 65yrs and those with intermediate risk cancer
- Non screen detected cases, criteria for local progression unreliable, high grade disease excluded, pathological stage not well detailed, morbidity form surgery high

Evolution of the *da Vinci* System

da Vinci Si

- Dual Console
- Enhanced HD Vision (1080i)
- Superior Ergonomics
- Increased Surgeon Control
- Scalable architecture
- Advanced instruments

da Vinci S

- 3D HD Vision (720p)
- Visual Inputs – TilePro
- Multi-quadrant access
- Streamlined set-up
- Procedure-specific and energy instruments

da Vinci Standard

- Eliminates lap compromises
- Introduction of 4th arm
- Simple instruments

Traditional Laparoscopy

INTUITIVE SURGICAL

Yaxley et al Lancet 2016;388:1057-1066

Robot Assisted Laparoscopic Prostatectomy vs Open Prostatectomy – Early Outcomes From a Randomised Controlled Phase 3 Study

- 151 open vs 157 robotic cases
- At 12 weeks – no difference in sexual, urinary and oncological outcomes
- Robotic prostatectomy associated with shorter Length of stay and decreased blood loss


da Vinci S

Perceived Advantages of Robotics

Improved instrumentation

3D magnified view of operative field

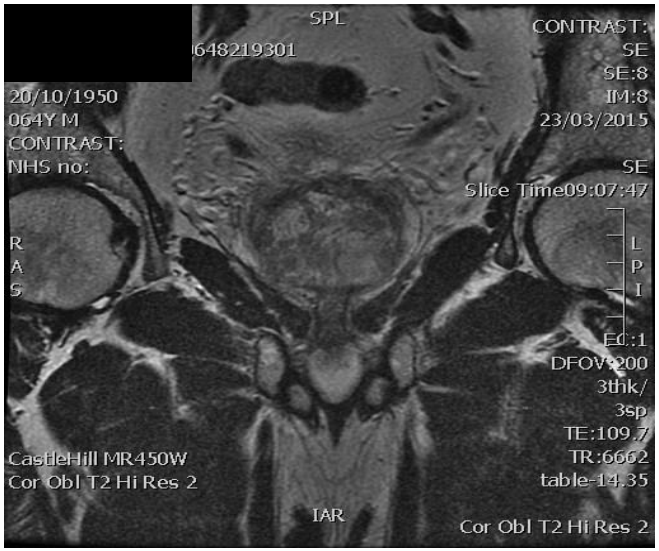
Less tremor

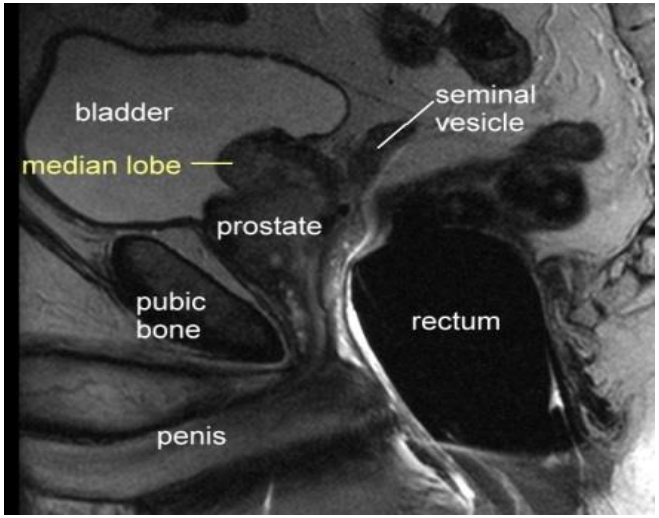
More consistency

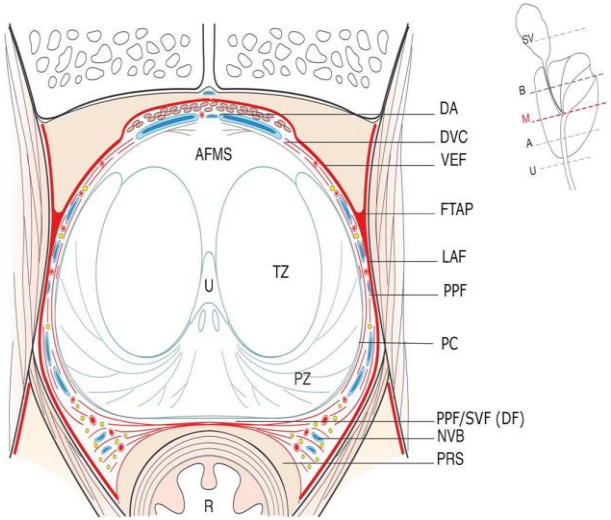
Ability to tackle more difficult cases

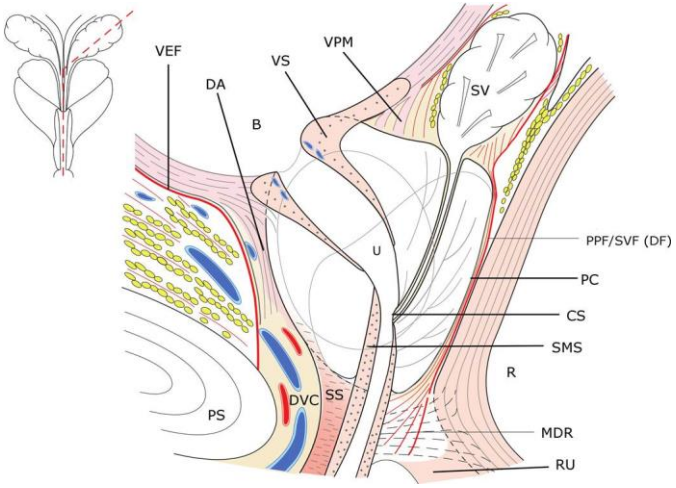
Ergonomic advantages

Why is MRI Useful

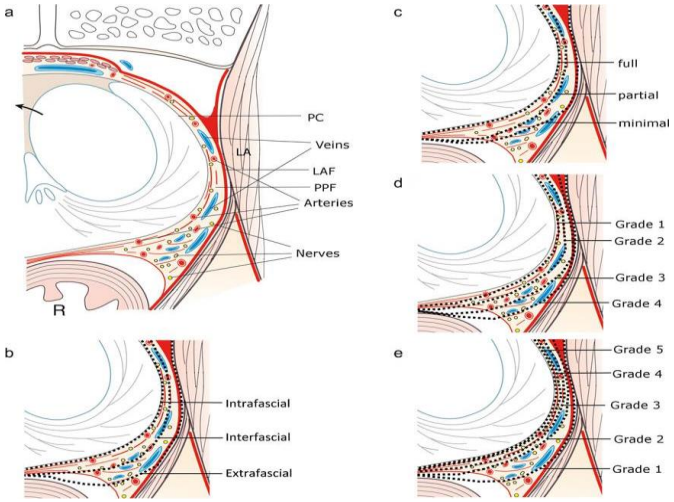


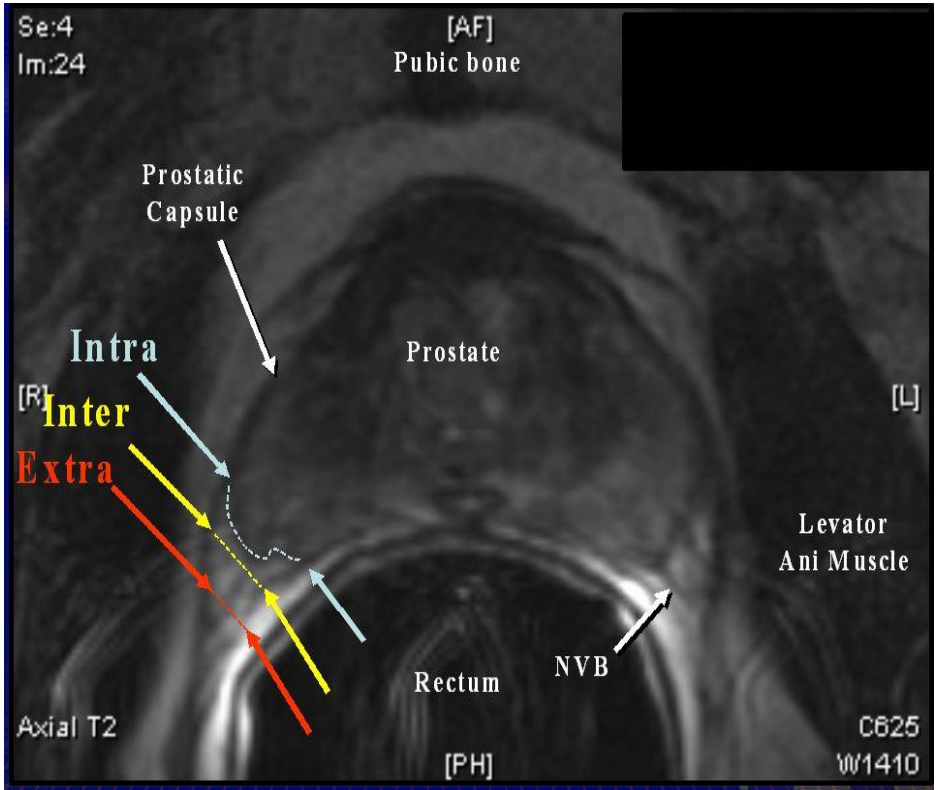



DA
DVC
VEF
AFMS
FTAP
LAF
TZ
U
PPF
PC
PZ
PPF/SVF (DF)
NVB
PRS
R
SV
B
M
A
U

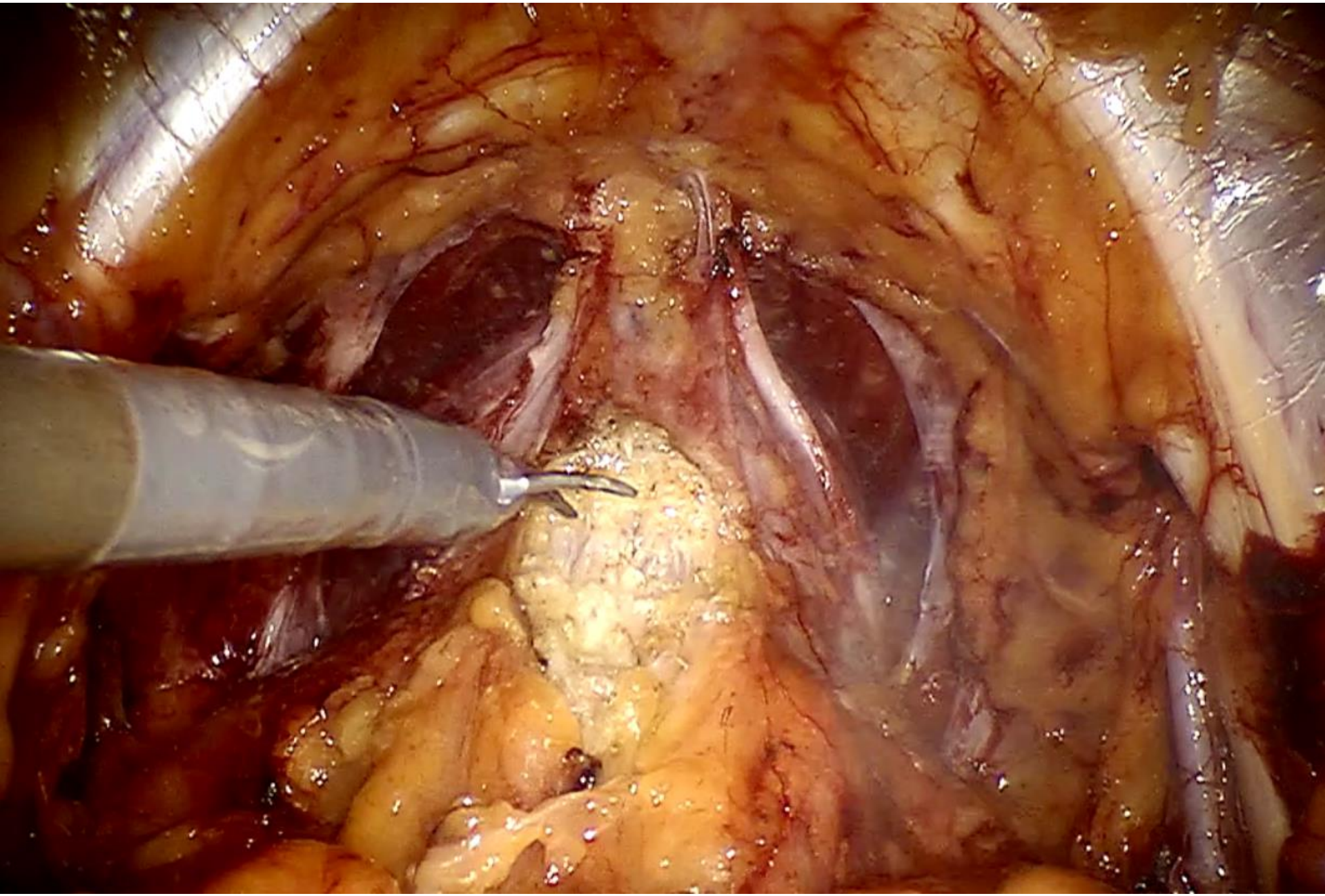

VEF
DA
VS
VPM
SV
B
U
PPF/SVF (DF)
PC
CS
SMS
R
PS
DVC
SS
MDR
RU

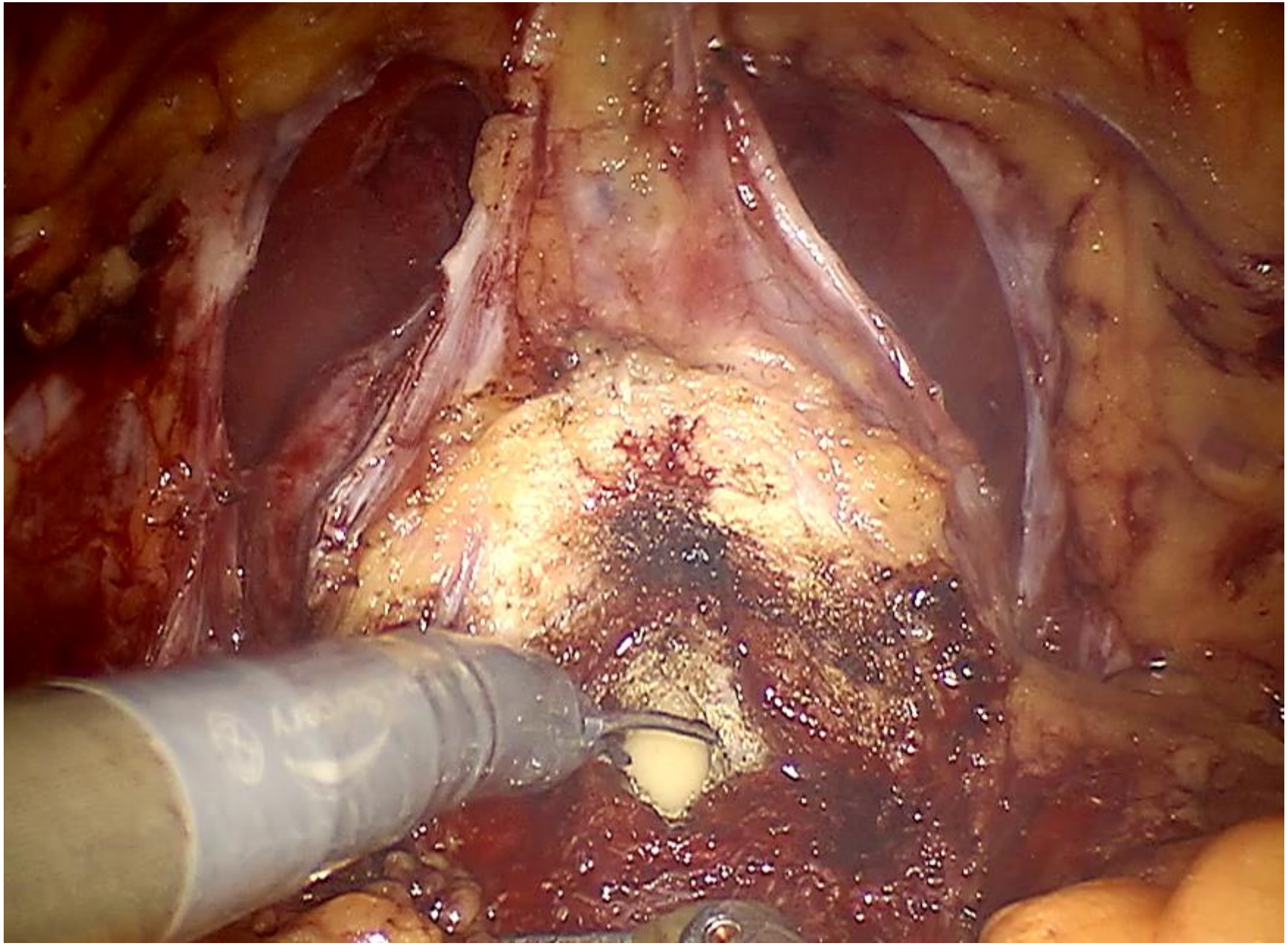

SBoyd
© MAYO 2004

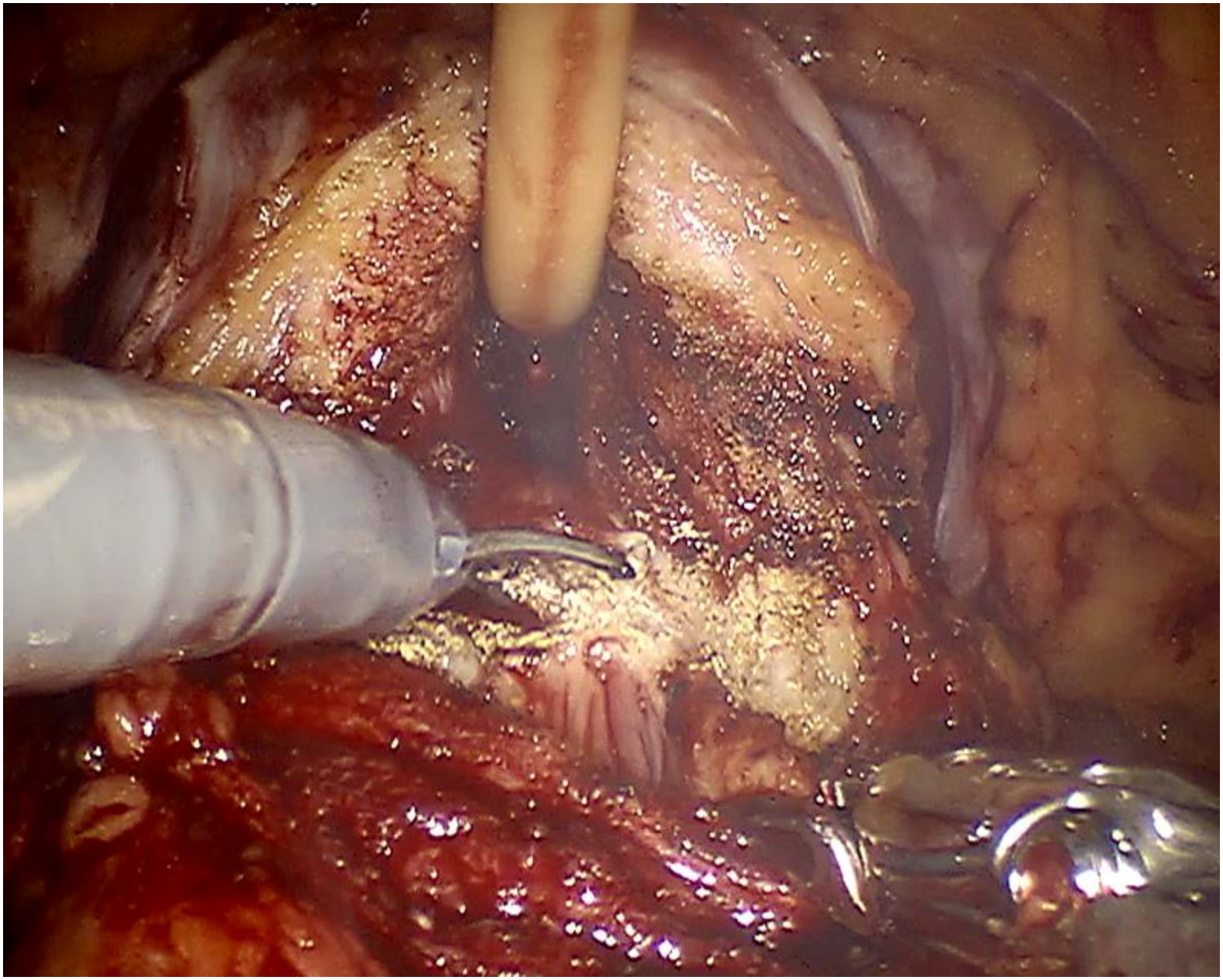

a
PC
Veins
LA
LAF
PPF
Arteries
Nerves
R
b
Intrafascial
Interfascial
Extrafascial
c
full
partial
minimal
d
Grade 1
Grade 2
Grade 3
Grade 4
e
Grade 5
Grade 4
Grade 3
Grade 2
Grade 1

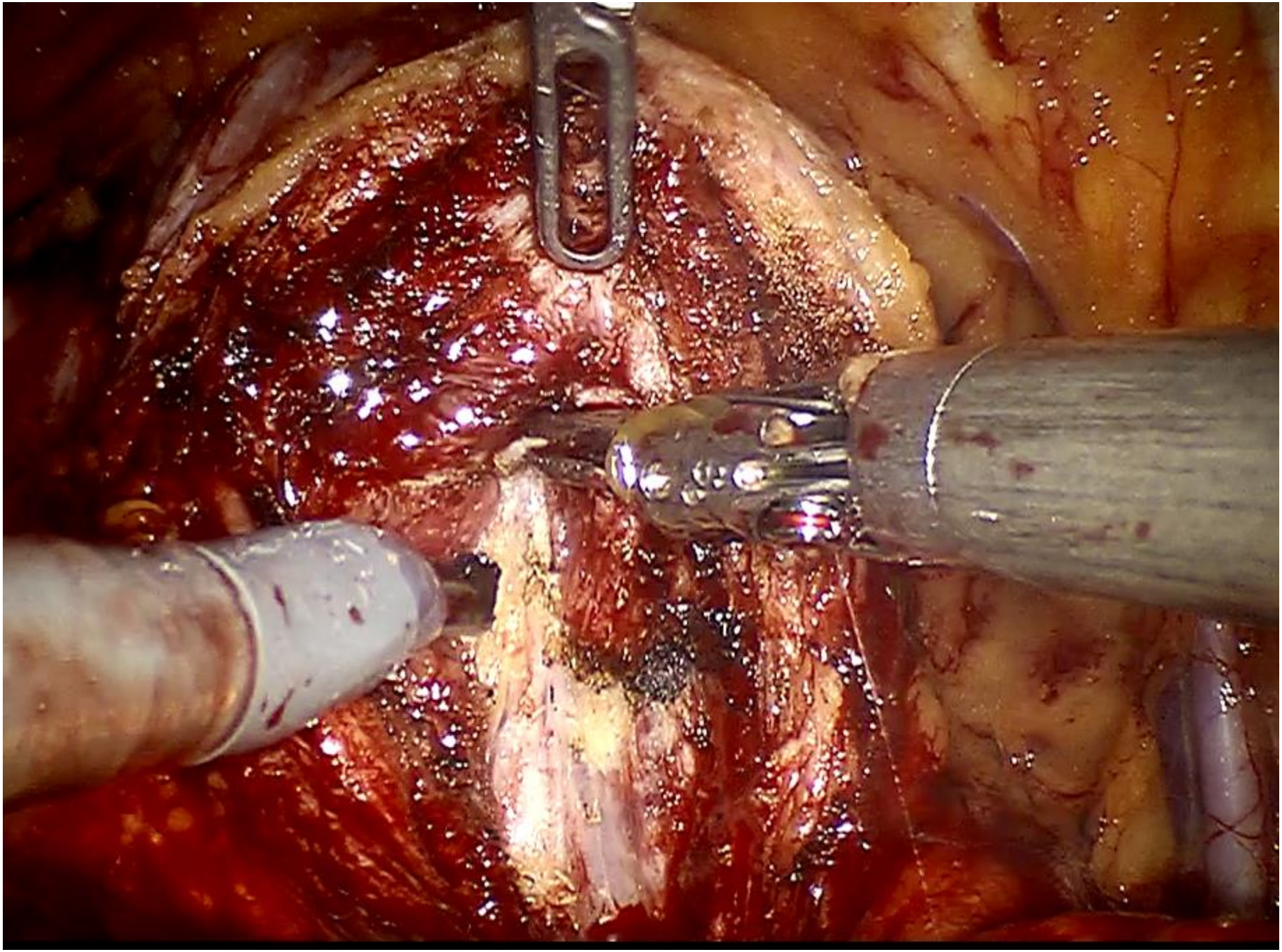


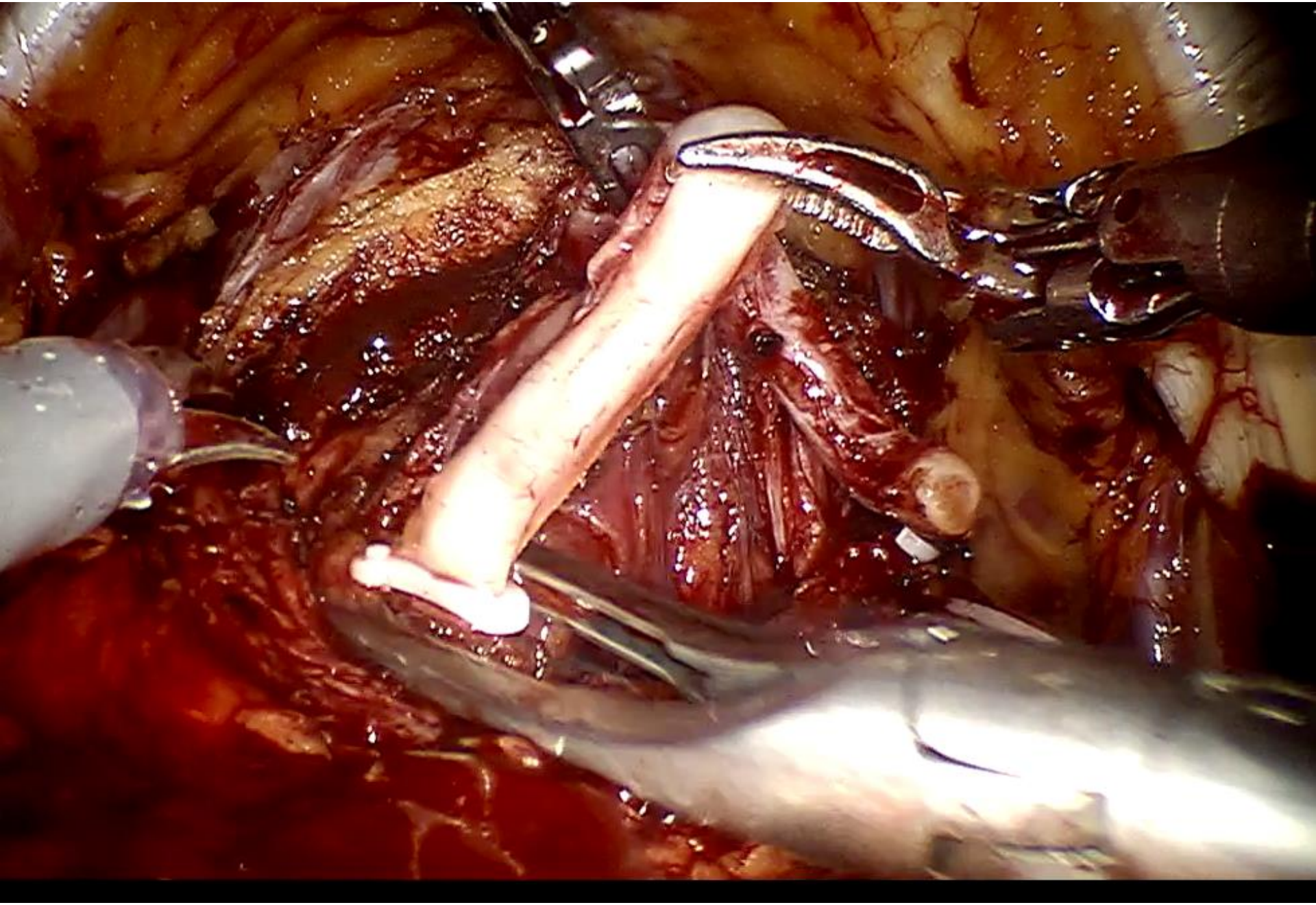
Endorectal MRI of prostate demonstrating the NVB and possible planes of dissection[7, 10]

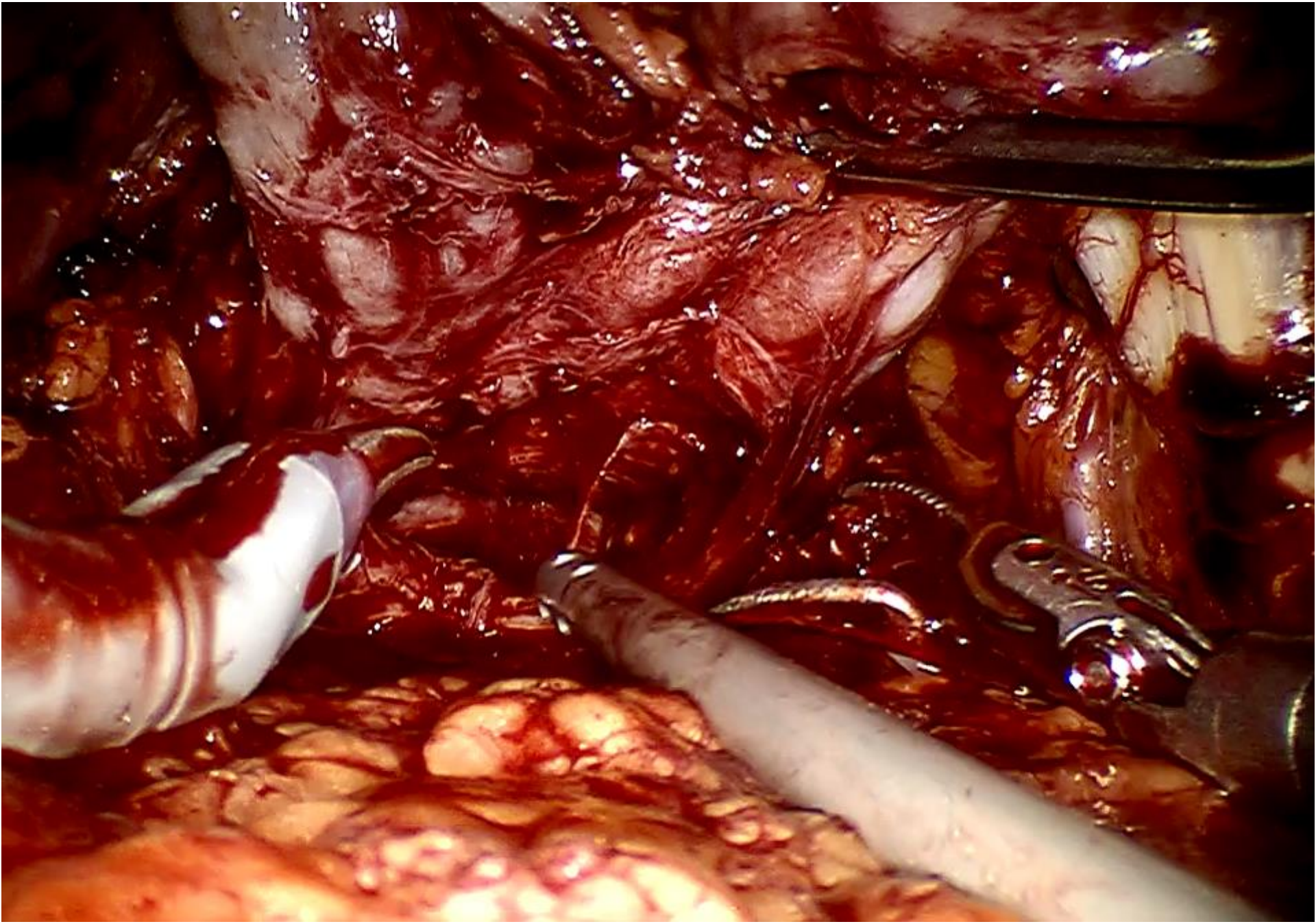


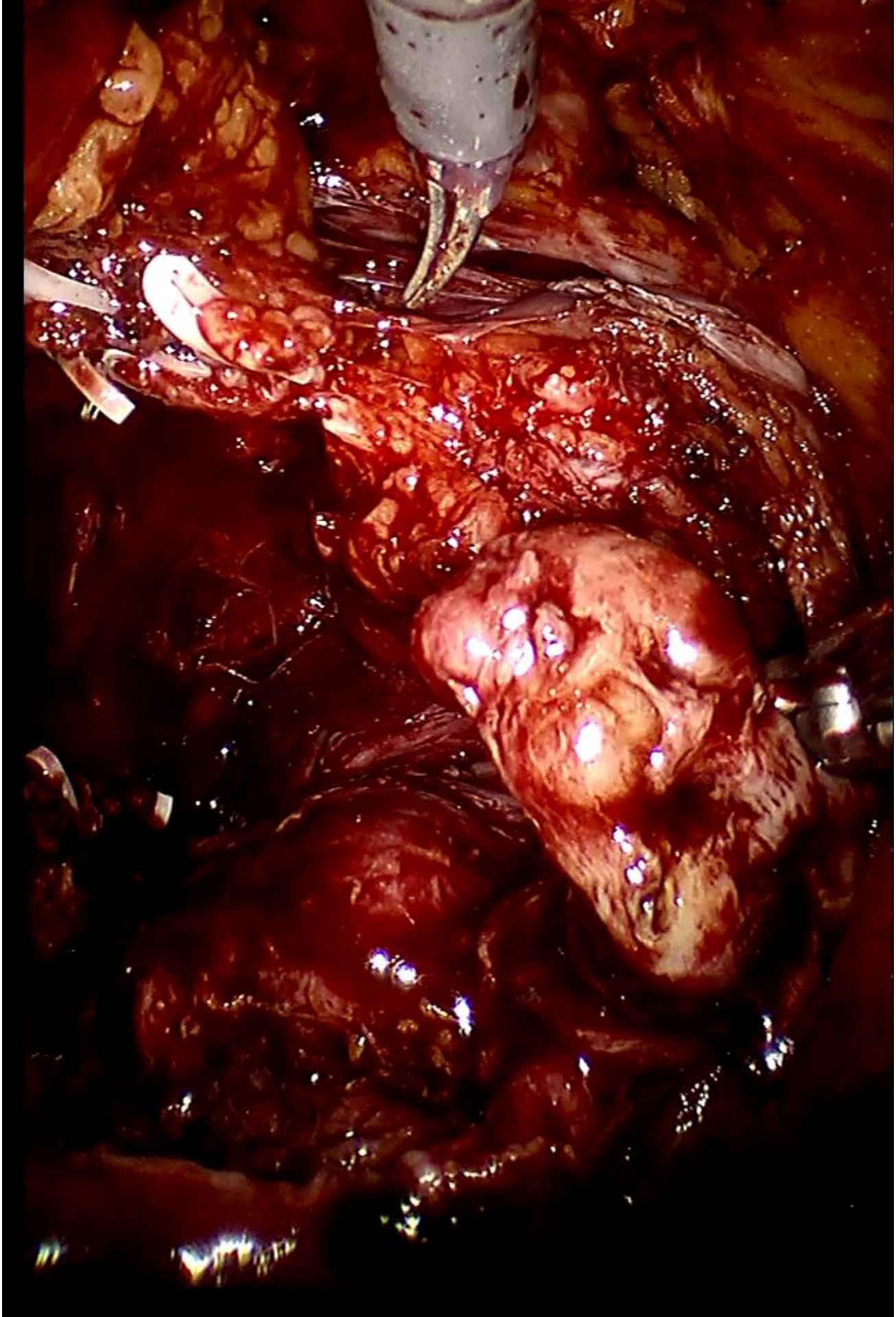


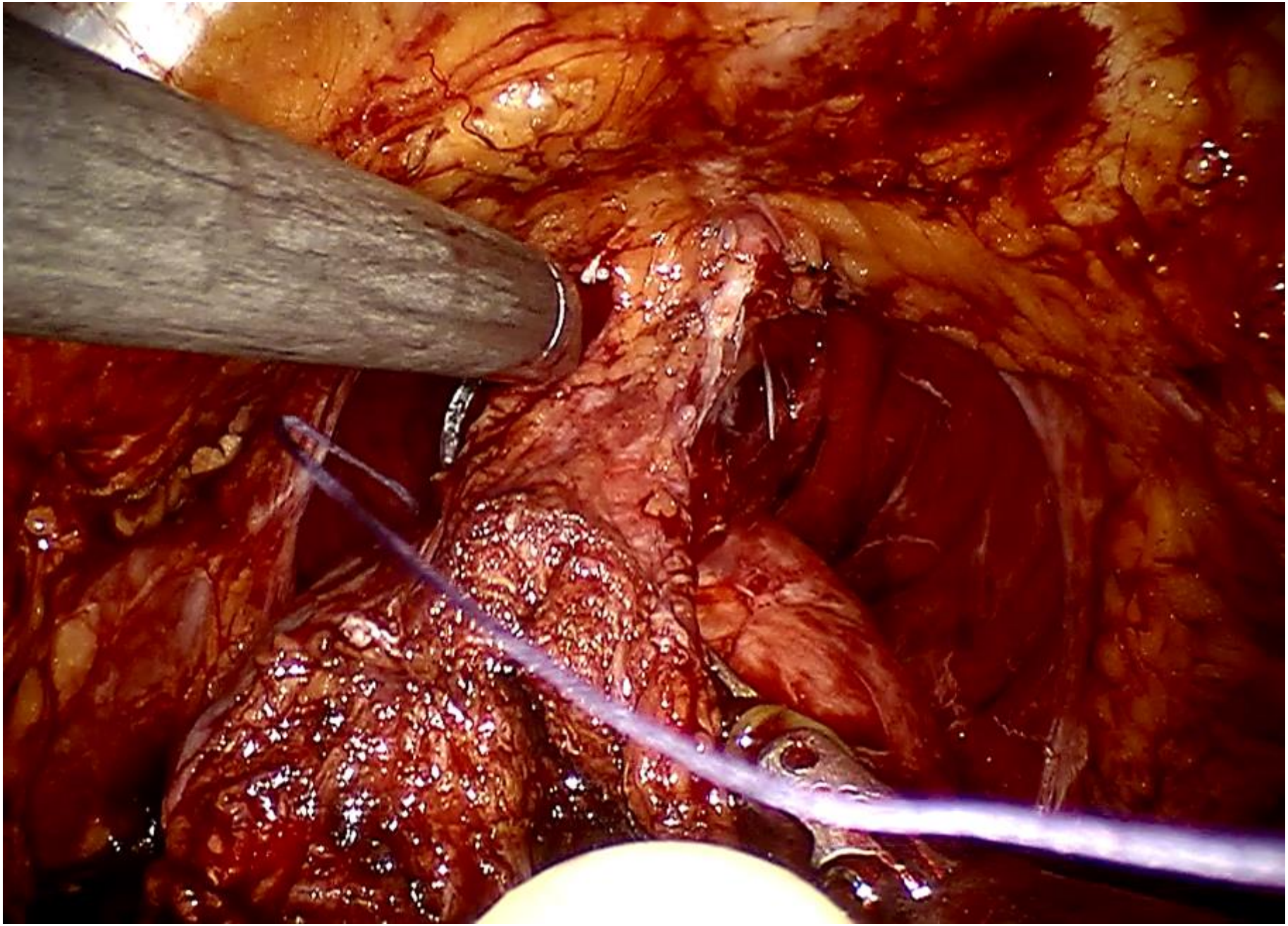


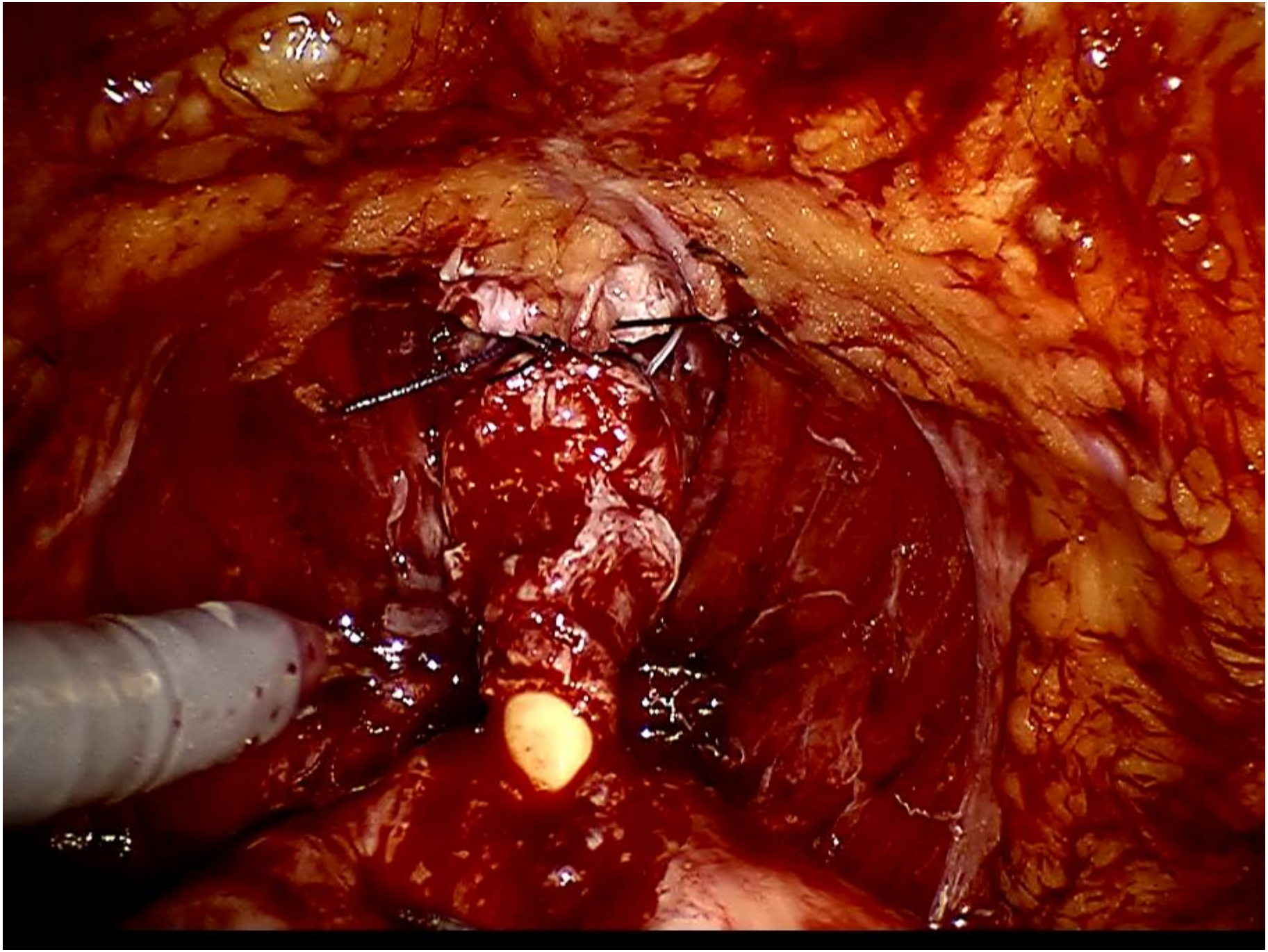


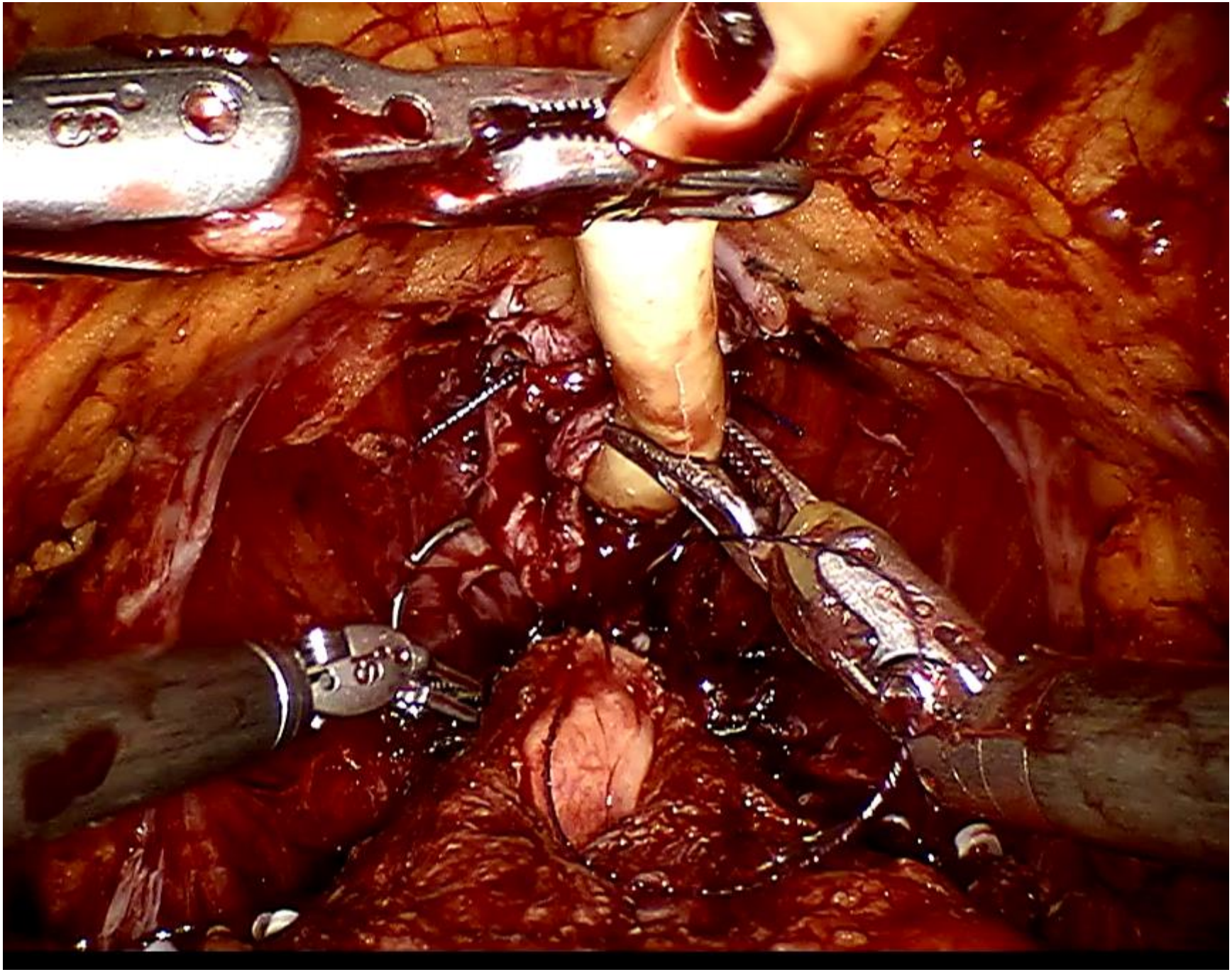


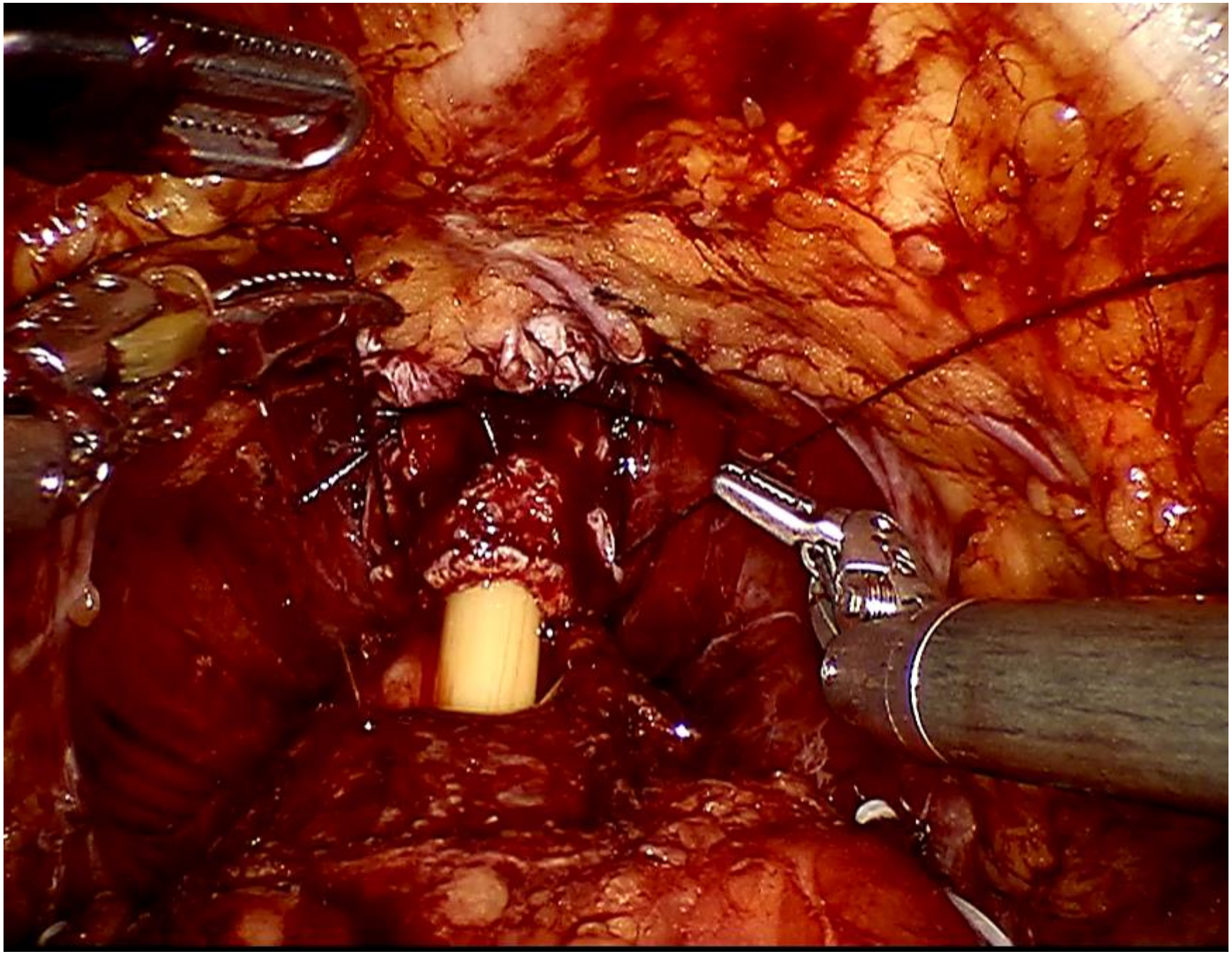


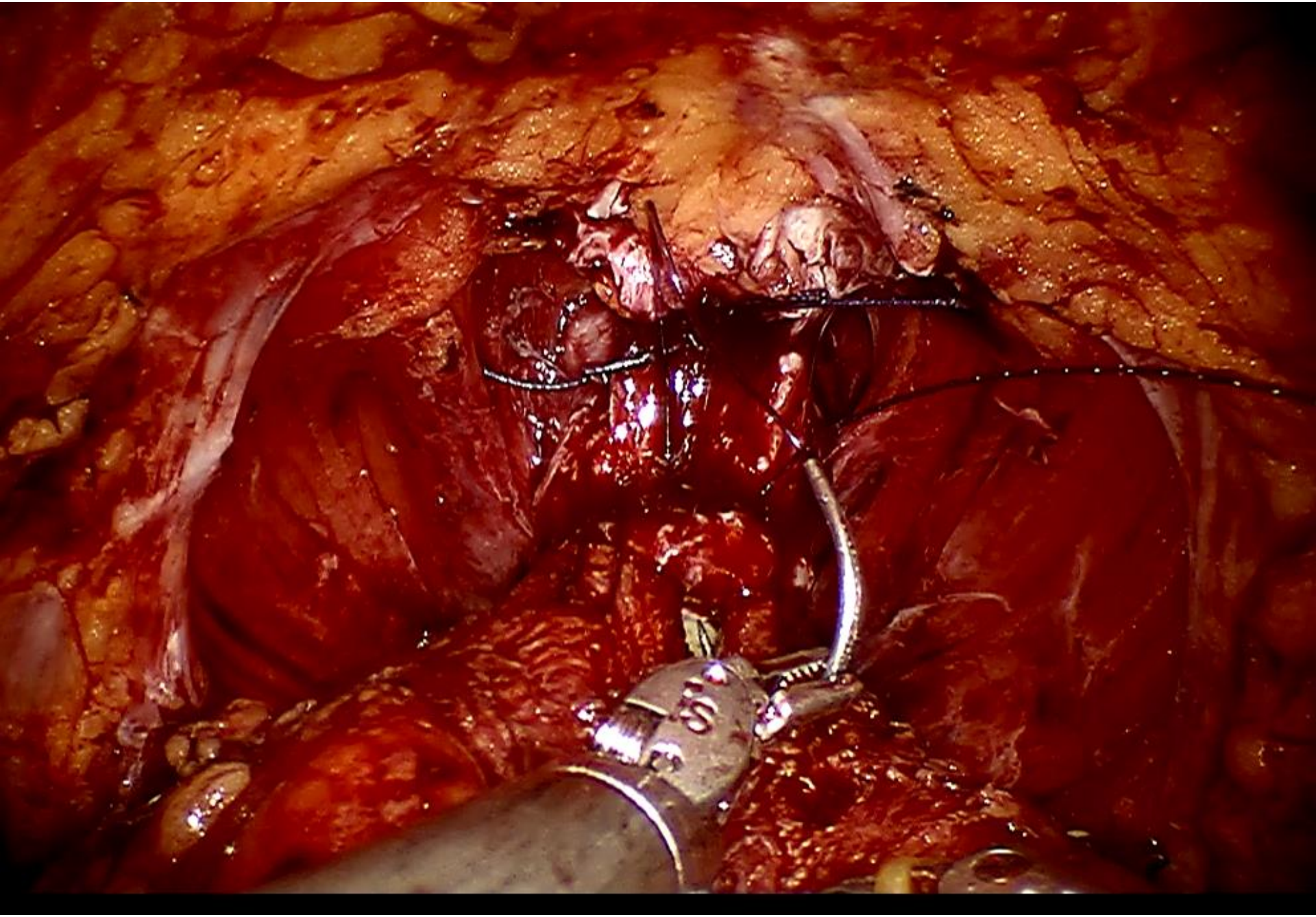












Complications

Complication	Incidence (%)
• Peri-operative death	0.0-2.1
• Major bleeding	1.0-11.5
• Rectal injury	0.0-5.4
• Deep venous thrombosis	0.0-8.3
• Pulmonary embolism	0.8-7.7
• Lymphocele	1.0-3.0
• Urine leak, fistula	0.3-15.4
• Slight stress incontinence	4.0-50.0
• Severe stress incontinence	0.0-15.4
• Impotence	29.0-100.0
• Bladder neck obstruction	0.5-14.6
• Ureteral obstruction	0.0-0.7
• Urethral stricture	2.0-9.0

Oncological Results of Radical Prostatectomy in Organ Confined Disease

Table 6: Oncological results of radical prostatectomy in organ-confined disease

Study	No. of patients	Mean follow-up (months)	5-year PSA-free survival (%)	10-year PSA-free survival (%)
Han et al. (2001) (39)	2404*	75	84	74
Catalona & Smith (1994) (40)	925	28	78	65
Hull et al. (2002) (41)	1000	53	-	75
Trapasso et al. (1994) (42)	601	34	69	47
Zincke et al. (1994) (43)	3170	60	70	52

* *15-year, 66%.*

Focal Therapy

- Analagous to “lumpectomy” in breast cancer
- Potentially preserves function
- Relies on prostate mapping via MRI and Biopsy
- Energy such as HIFU and cryotherapy have been used
- Regarded as experimental and oncologically dubious by some

Locally Advanced Prostate Cancer

- Role of Surgery
- Role of Radiotherapy (Ext beam / Ext beam+HDR brachytherapy)
- Role of Combination Treatment
- ?Role of chemotherapy

Metastatic Disease

- Hormone therapy
- Docetaxel chemotherapy
- Cabazitaxel chemotherapy
- Novel second line androgens (enzalutamide and abiraterone)
- Radium-223
- Sipleucel -T

Summary

- Prostate cancer treatment depends on accurate diagnosis, staging and should be individualised to every patient
- In line with advances in diagnostics, there have been significant oncological advances over the last few years
- These treatments are likely to be integrated into pathways at an earlier stage in the future