



En-bloc TUR: does it really make a clinically significant difference?

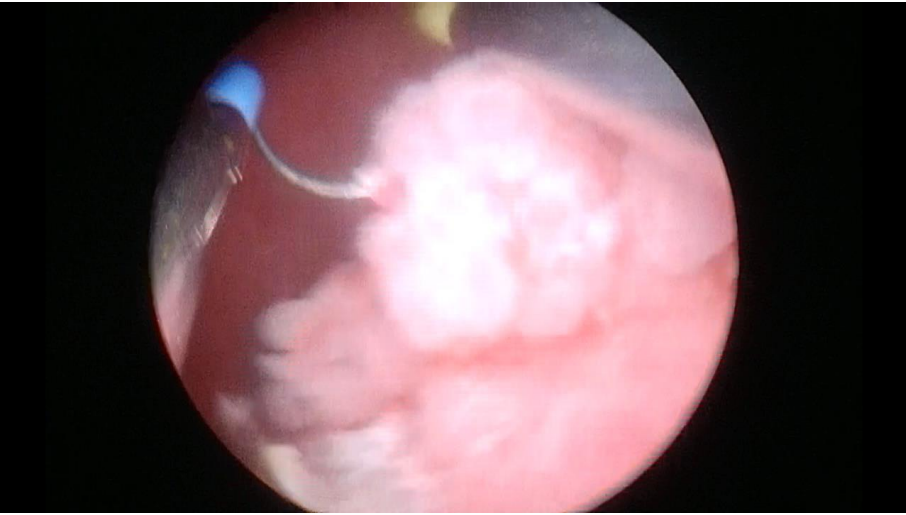


M. P. Laguna

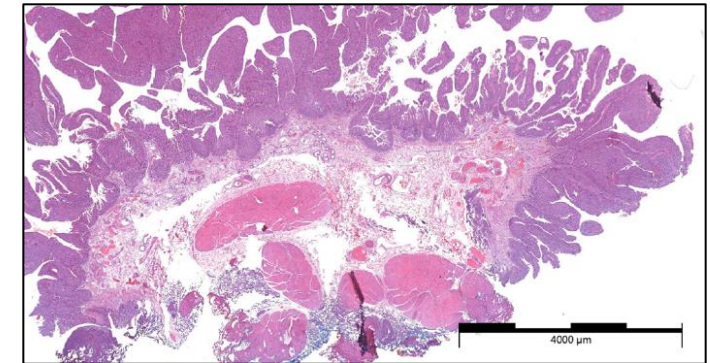
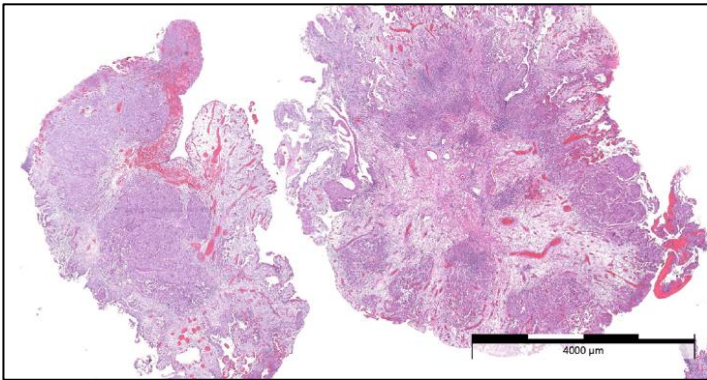
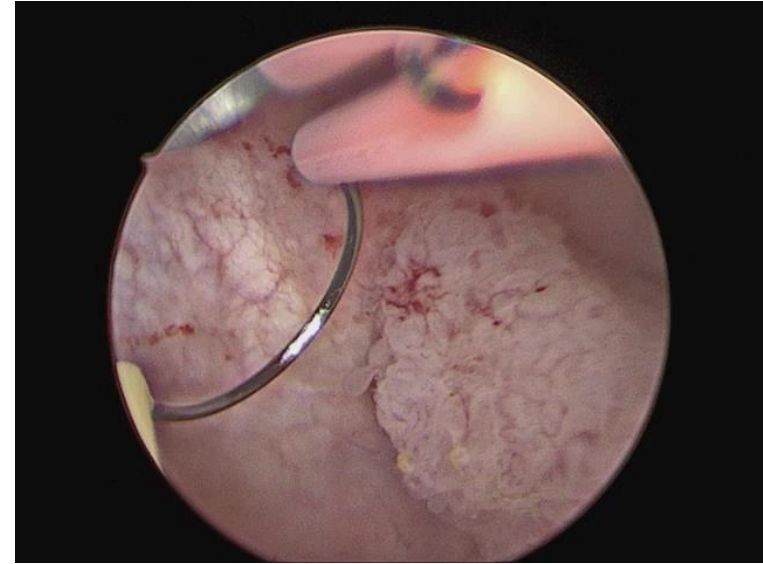
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TURBT vs ERBT



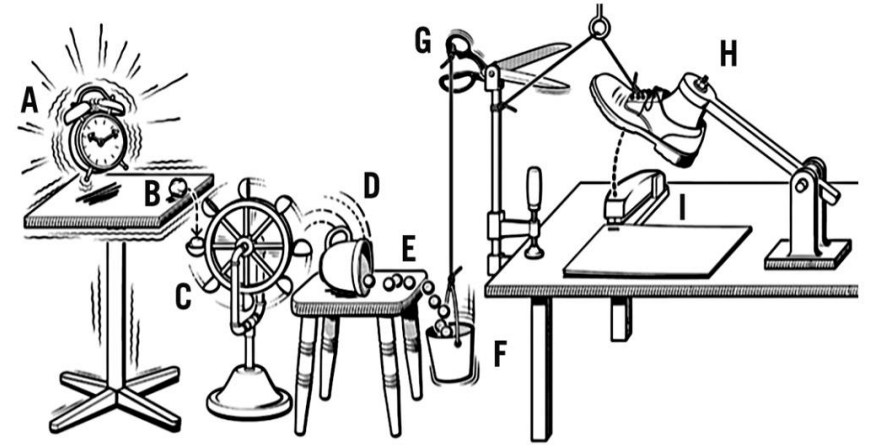
- Optimize the quality of histopathology
- Respect the oncological principles
- Provide detrusor muscle
- Reliable staging & substaging
- Minimize the risk of residual tumor
- Reliable prediction of recurrence rates
- Reduces the recurrence rates
- Reduce the complication rate



ERBT: a hip or a ragged trend?

- **Retrospective and case control** (hypothesis generating)
- **Several consensus** (expert opinion, identifying gaps)
- **Several small RCT** (Ideal design? / flaws? /generalizable?)
- **Systematic Reviews** (quality depending on article type)
- **One Umbrella review** (re-analyze and individual metanalyze each SRs)

The concept of causality

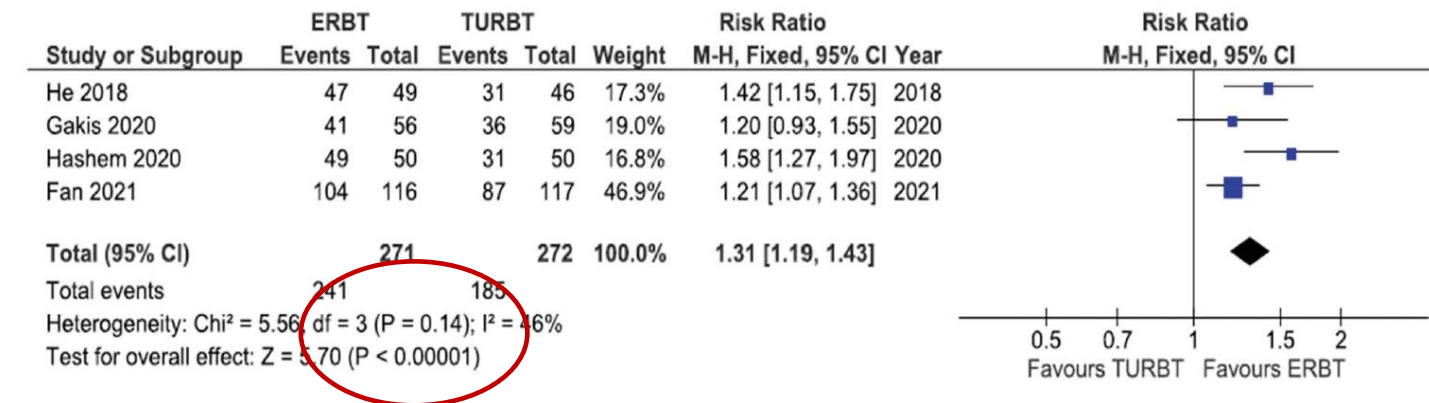


In an experimental setting (e.g. RCT), a causal relationship between a specific factor and a particular outcome may consistently occur.

However, it may not necessarily persist outside the RCT context

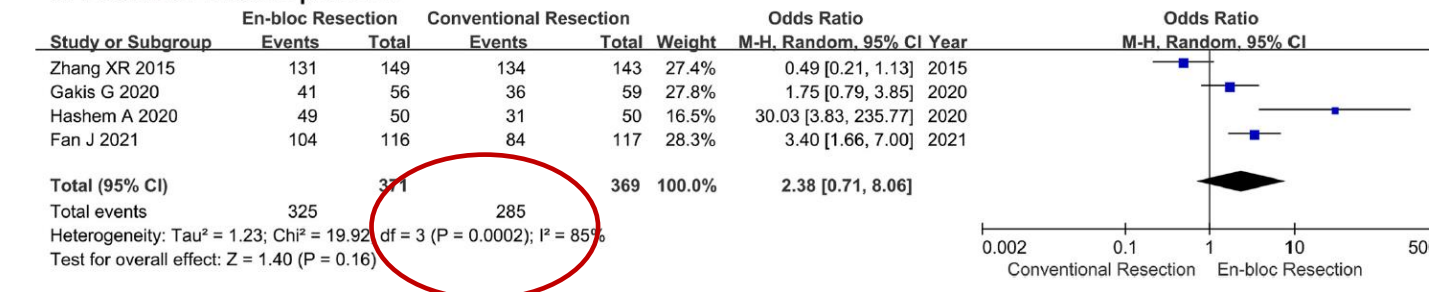
Systematic Reviews of RCTs

(A) DM presence in RCTs

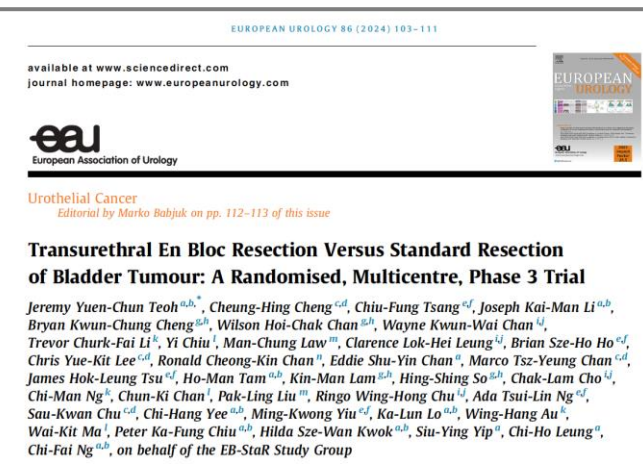
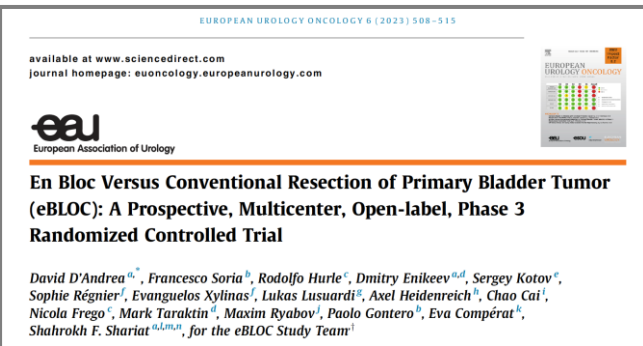
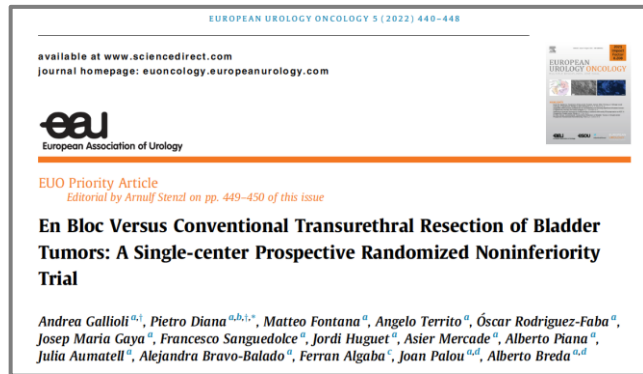


- Is ERBT feasible? YES
- Current quality of evidence do not allow for solid conclusions
- Is it superior to conventional TURBT ?

C. Detrusor muscle present



Trial Design and Endpoints



Primary endpoint: DM presence in the pathological specimen

Secondary endpoints: staging of BC, AJCC-TNM- WHO, the feasibility of T1 subclassification (T1a/b/c), rate of artifacts in specimen, operative variables, post op complications (Clavien-Dindo) and early oncological outcomes

Primary endpoint: quality of the pathologic specimen (DM specimen)

Secondary endpoints: bladder perforation, persistent disease at second-look TURB, + lateral and deep resection margins, operation time, obturator reflex, conversion to cTURB, RFS at 3 mo.

Primary outcome: 1-yr recurrence rate

Secondary outcomes: DM in specimen, obturator reflex, operative time, LoS, 30-d complications, residual disease or upstaging at second-look TURB and 1-yr progression rate

Random



Power calculation based on different assumptions



Only Hong- Kong trial double-blinded



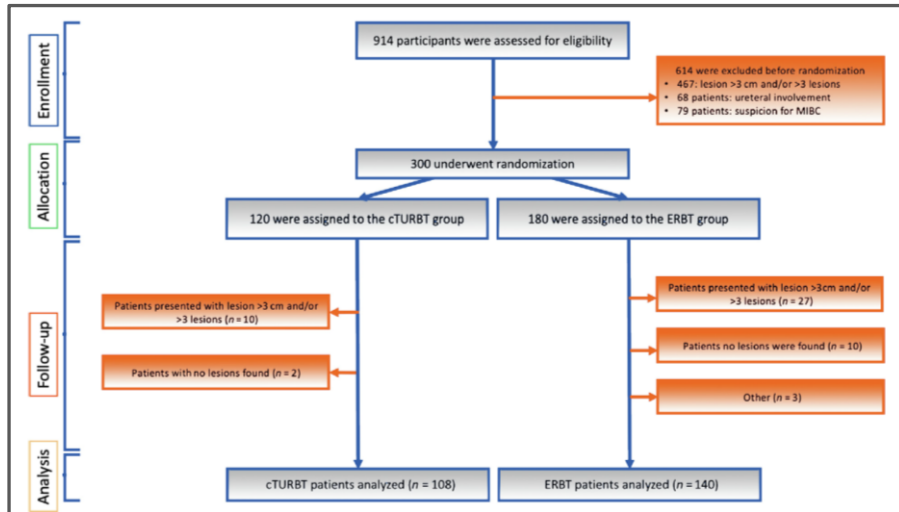
Patient selection



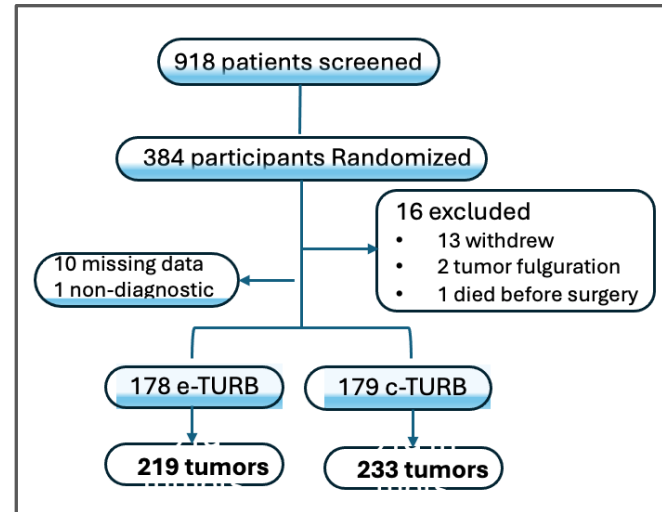
	Gallioli A et al.	d'Andrea D et al.	Teoh JYC et al.
Inclusion	<ul style="list-style-type: none"> • Tumors up to 3 cm • Maximum 3 tumors • <i>Primary & recurrent</i> 	<ul style="list-style-type: none"> • <i>Primary Tumors 1-3 cm</i> • Maximum 3 tumor • <i>Expected NMIBT</i> 	<ul style="list-style-type: none"> • Tumor base \leq 3 cm • No limit in number • <i>Primary & recurrent</i>
Exclusion	<ul style="list-style-type: none"> • Preoperative evidence of MIBC • Evidence of UTUC • Ureteral involvement • Suspicion of N+ • Metastatic extension 	<ul style="list-style-type: none"> • Previous/ Synchronous history of UTUC • Life expectancy of <1 y • Pregnancy • Cross sectional imaging no mandatory 	<ul style="list-style-type: none"> • Detected during BCG • Other than NMIBC • Non Urothelial cancer • Previous UTUC • ECOG 3 • ASA \geq III • Bleeding disorder • Pregnancy • Active malignancy • Life expectancy <1 yr

Patients Flow diagram (CONSORT)

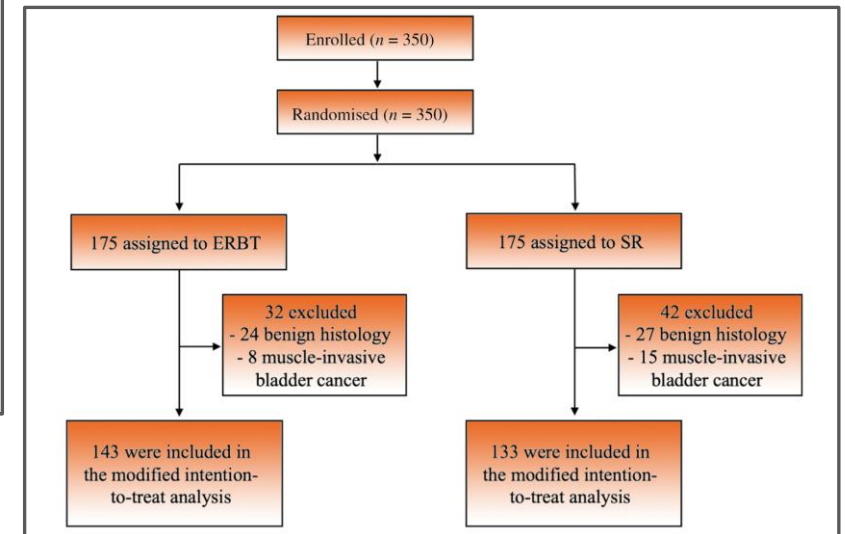
Spanish trial (248 patients)



International trial (357 patients , 452 tumors)



Hong Kong trial (276 patients)



- Inclusion of 25% of screened patients
- Two of the trials did not include planned sample
- Subgroup analysis not sufficiently powered in any of the trials
- Type of RCT only described in one trial

Patients characteristics at baseline

- At baseline, no differences between groups in any trial
- Variables reported at baseline varied among trials
- Age was slightly different in the 3 trials



	Spanish trial	International trial	Hong Kong trial
Low grade	ERBT 50% cTURB 52%	ERBT 63% cTURB 54%	ERBT 64% cTURB 70%
High grade	ERBT 39% cTURB 38%	ERBT 33% cTURB 43%	ERBT 31% cTURB 28%
Risk groups		Not reported	
• <i>Low</i>	ERBT 8% / cTURB 11%		ERBT 31% / cTURB 34%
• <i>Intermediate</i>	ERBT 51% / cTURB 39%		ERBT 45% / cTURB 56%
• <i>High</i>	ERBT 33% / cTURB 44%		ERBT 23% / cTURB 18%

**Variations in tumor size, number of tumors,
primary/recurrent rates/ Grade and risk groups**

Clinical Relevant Outcomes

	Spanish trial		International trial		Hong Kong trial	
	ERBT	TURBT	ERBT	TURBT	ERBT	TURBT
Successful ERBT	95%	-	96%	-	88%	-
Complications	21%	24%	15%	13%	-	-
• Blader perforation	20%	17%	5.6%	12%	-	-
• Obturator reflex	11%	6.5%	8.4%	16%	26%	19%
• Median operating time	30 min	30 min	26 min	25 min	28 min	22 min *
• Median irrigation time	0.5 d	0.5 d	-	-	-	-
• Median bladder catheter	2 d	2d	-	-	-	-
• Median LoS	2d	2 d	-	-	2 days	2 days

*Statistically significant

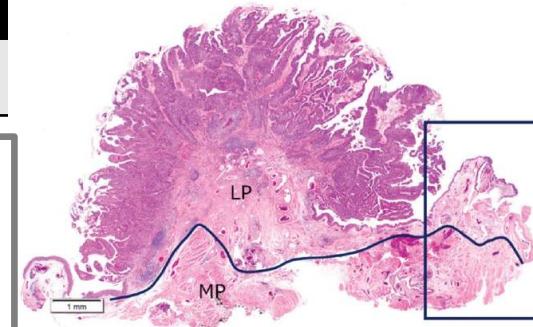
No differences in complications between ERBT and cTURBT

Clinical Relevant Pathology

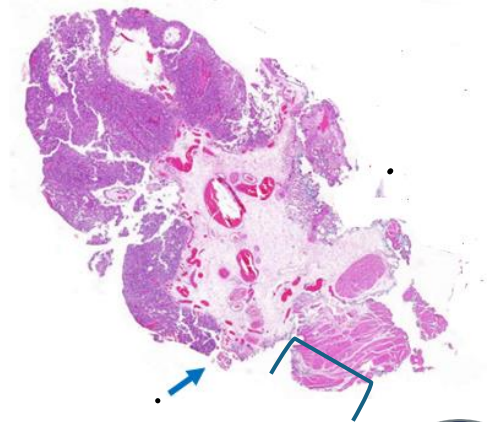


	Spanish trial		International trial		Hong Kong trial	
	EBRT	cTURBT	EBRT	cTURBT	EBRT	cTURBT

- ***Deep resection margin evaluable in 69 % and 52.4% of ERBT and cTURB respectively**
- **** Lateral resection margin evaluable in 64% and 38.2% of ERBT and cTURB respectively**
- **Second look was not systematically performed in all R1 patients (disease found in 20% to 50% of patients)**




(Yanigisawa T et al. J Urol, 2021; 206: 252-259)



A glimpse in the margins evaluation

**THE JOURNAL
of UROLOGY**
www.auajournals.org/journal/uro

Clinical Significance of Horizontal and Vertical Margin of En Bloc Resection for Nonmuscle Invasive Bladder Cancer

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ORIGINAL ARTICLE

En-bloc resection of bladder tumors for pathological staging: the value of lateral margins analysis

Ahmed EISSA ^{1,2}, Ahmed ZOEIR ^{1,2}, Silvia CIARLARIELLO ¹, Luca SARCHI ¹, Maria C. SIGHINOLFI ¹, Ahmed GHAITH ², Stefano PULIATTI ¹, Raffaele INZILLO ¹, Luca REGGIANI BONETTI ³, Mino RIZZO ¹, Bernardo ROCCO ¹, Salvatore MICALI ^{1*}

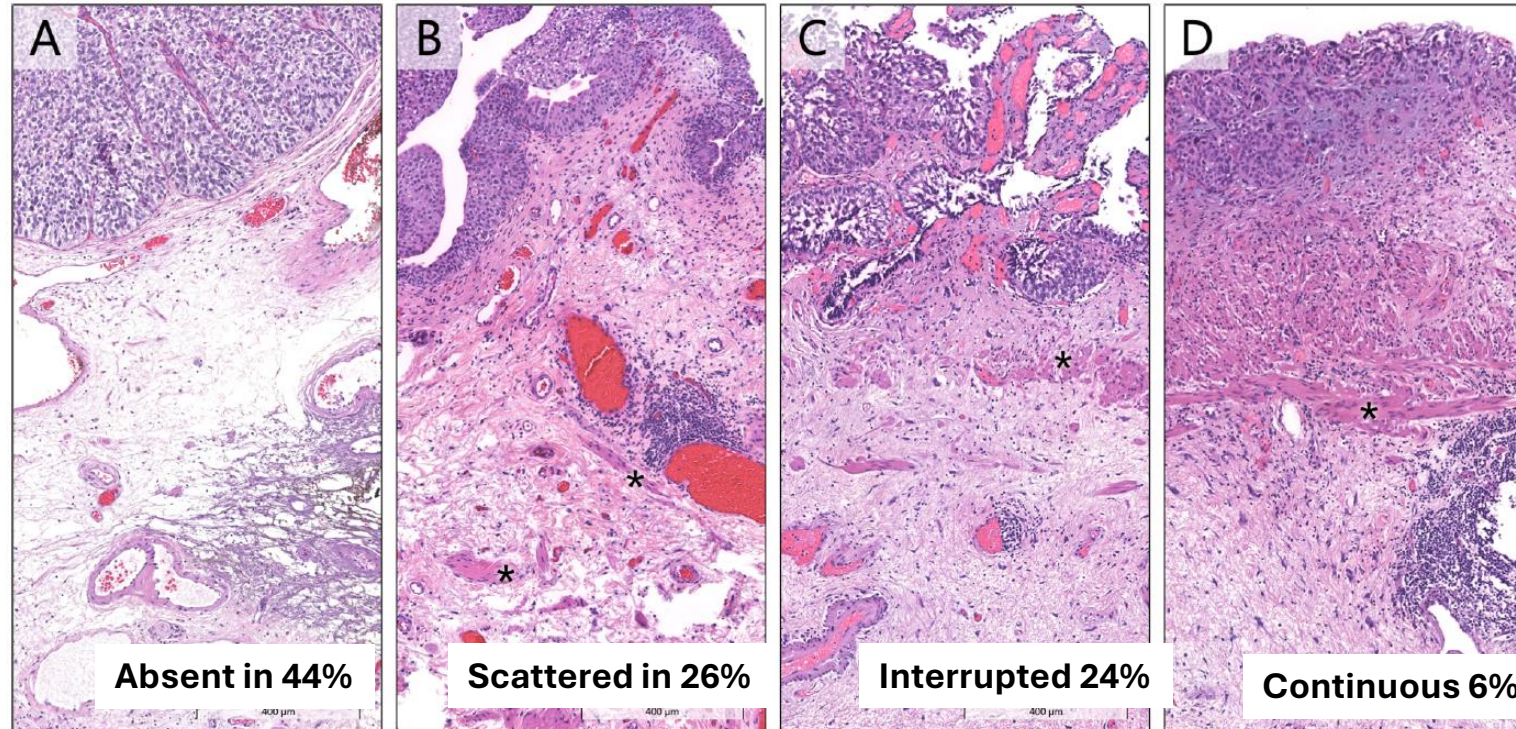
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- Detrusor present in $\approx 90\%$ of patients
- Diagnostic horizontal margin diagnosis is possible in 63%-86% of patients
 - Tumor at horizontal margin found in up to 45% of cases
 - Dysplasia found in 1/3 of cases
- Diagnosis vertical margin possible in 99%
 - Rarely positive for tumor
- No different recurrence between + or - mucosal margins

Variants on the presence of MM



MM identified in 70% of EBRT vs 27% in cTURBT

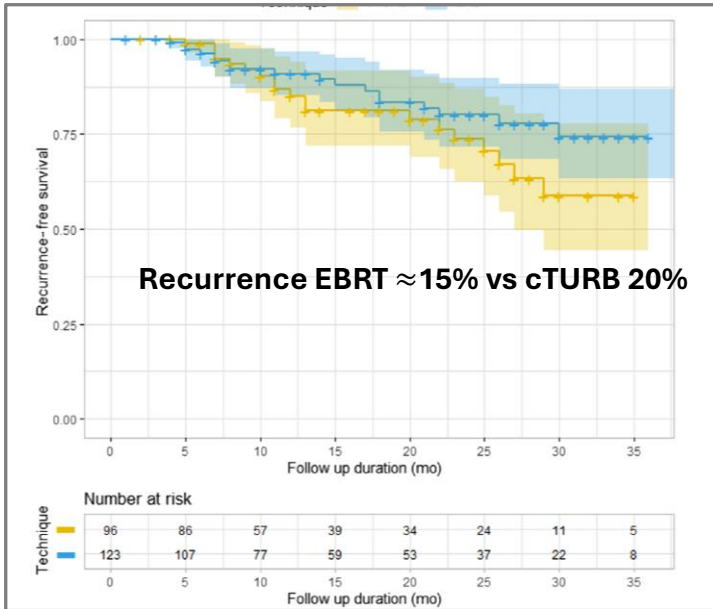
Tumor size is a relevant factor in the preservation of “*en bloc*” architecture

Size between 1-2 cm = higher rate of preserved architecture in EBRT

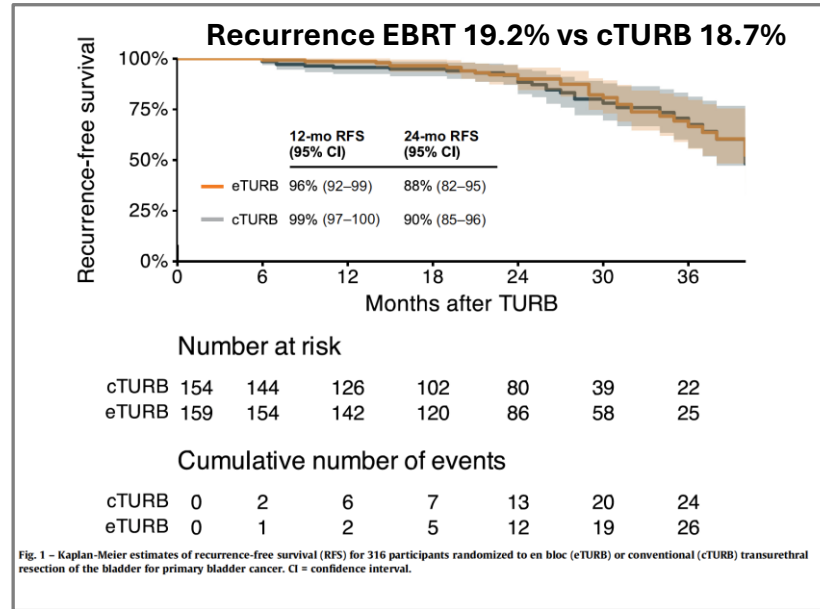
(Struck J P et al. Adv Ther , 2021: 38 / Ling H et al. WJ Urol, 2019: 37)

Oncological outcomes

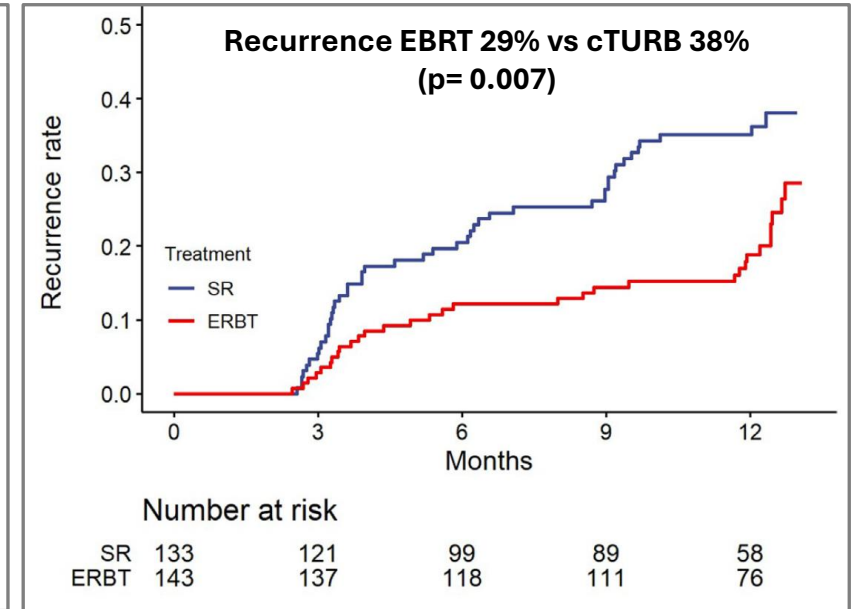
Spanish trial (median follow up 15 mo)



International trial (median follow up 24 mo)



Hong Kong trial (at 12 mo)



Subgroup analysis
Patients that benefit from ERBT



- Tumors 1-3 cm
- Single tumor
- Ta disease
- Intermediate-risk

Conclusions

- Besides making your pathologist happy.....
- Candidates to ERBT are only patients with tumors between 1-3 cm in size and multiplicity limited to 3 tumors,
- There is moderated evidence that EBRT decreases the intraoperative undesired events, the length of stay and the rate of residual tumor when compared with cTURBT (subgroups analysis of RCTs not powered),
- There is low evidence that ERBT increases the rate of DM in the pathology specimen.
- Recently, for the first time a RCT has shown superiority of ERBT vs cTURBT in decreasing 1-year recurrence in tumours of 1-3 cm in size, single, Ta and of EAU intermediate-risk (LoE 1b),

At the present, EBRT will entail clinical relevance for those centers with a low rate of DM in the cTURBT and for those patients with a solitary tumor, of 1 to-3 cm of size and suspected to be a Ta.



