

Eradication of *Pseudomonas aeruginosa* Biofilm in Endotracheal Tubes Based on Lock Therapy: Results From an In Vitro Study

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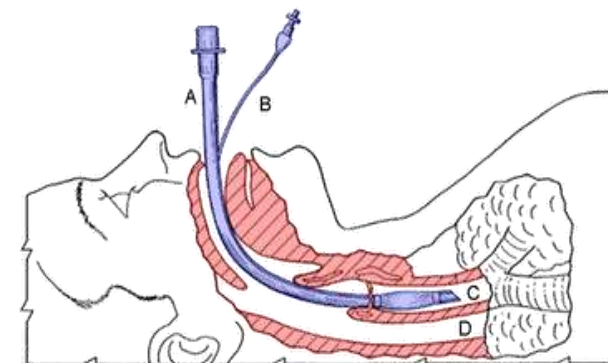


BACKGROUND

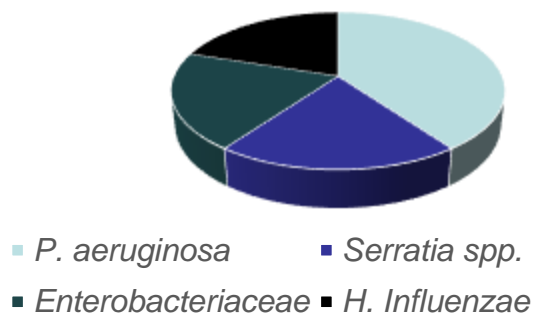
❖ **Ventilator-Associated Pneumonia (VAP)** accounts for **22%** of hospital –acquired infections^{1, 2}.

❖ Up to **27%** of intubated patients develop VAP (**46%** in **critical care** patients with >48h of MV)³.

❖ Overall VAP-ICU rate in **HGUGM 2016**: 7 episodes/1,000 days of MV.



Etiology of VAP
HGUGM-2016



Clinical impact

- Attributable **mortality** rate: 13%⁴.
- Extra days of **MV**: 7-11¹.
- Extra days of **hospitalization**: 11-13¹.
- Associated **costs**: 11,000€ (Spain)-40,000\$ (USA)^{5,6}.

¹ Kalil et al. Clin Infect Dis 2016.

² Magill SS et al. N Engl J Med 2014.

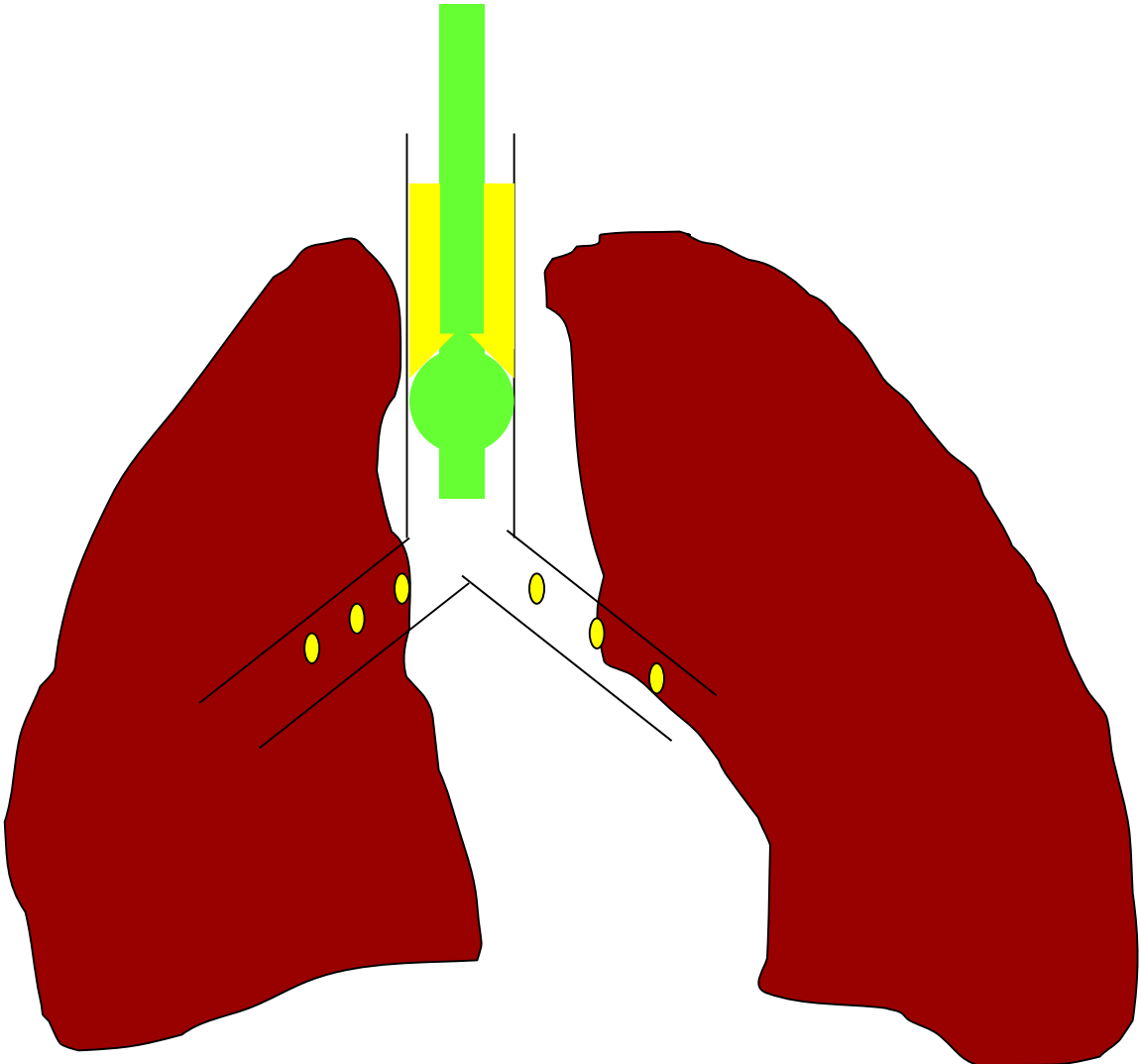
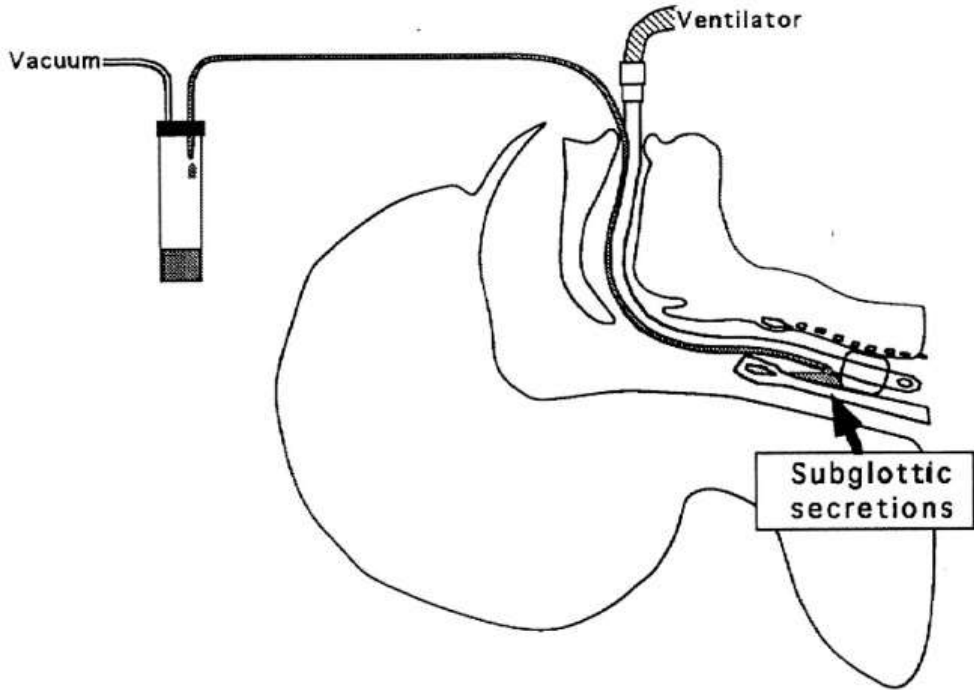
³ Hortal J et al. Crit Care 2009.

⁴ Ralsen WG et al. Lancet Infect Dis 2013.

⁵ Riu et al. Enferm Infecc Microbiol Clin. 2012.

⁶ Kollef MH et al. Infect Control Hosp Epidemiol 2012.

BACKGROUND



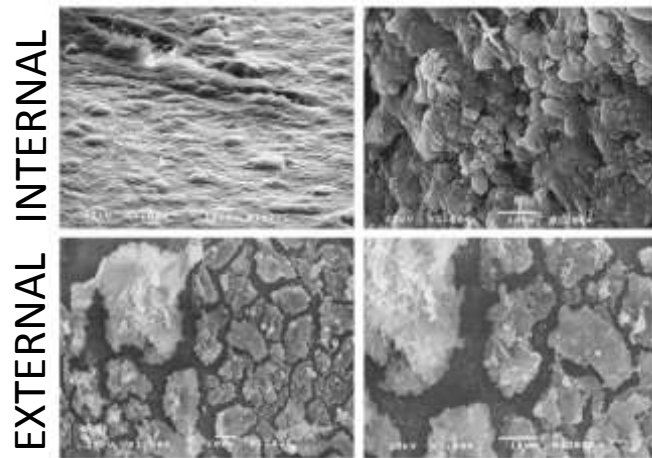
BACKGROUND

- ❖ Bacterial **biofilm** plays an important role in the pathogenesis of VAP^{1,2,3,4}.
- ❖ Advanced ETT biofilm **stage** is related to VAP (not days of MV)^{5,6,7,8}.

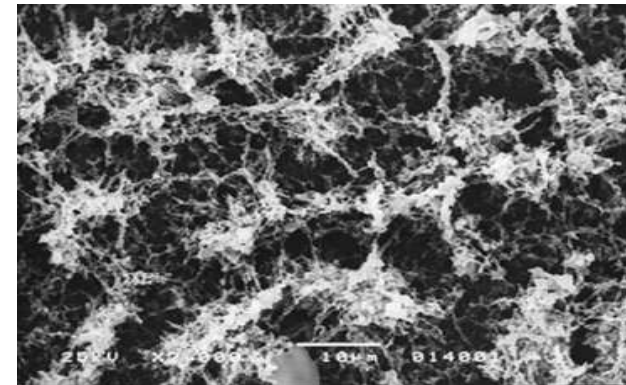
MICROSCOPY RESEARCH AND TECHNIQUE 77:305-312 (2014)

Endotracheal Tube Biofilm and Ventilator-Associated Pneumonia With Mechanical Ventilation

PAULA REGINA DE SOUZA,¹ DENISE DE ANDRADE,² DANIELLE BEZERRA CABRAL,² AND EVANDRO WATANABE^{3*}



honeycomb structure



S. epidermidis *P. aeruginosa*

¹ Inglis et al. J Clin Microbiol 1989..

² Sottile et al. Crit Care Med 1986.

³ Gil-Perotin et al. Crit Care 2012.

⁴ Hoiby et al. Clin Microbiol Infect 2015

⁵ Wilson et al. J Trauma 2012

⁶ Azmy et al. Ultrastruct Pathol 2017.

⁷ Friedland et al. Arch Otolaryngol Head Neck Surg 2001.

⁸ Danin et al. Respir Care 2015.

PREVENTIVE MEASURES in HGUGM

- ✓ Continuous training
- ✓ Hand hygiene
- ✓ Subglottic aspiration (100 mm Hg) ^{1,2,3}
- ✓ Continuous cuff pressure monitoring (25 cm H₂O)
- ✓ Position (30-45°)
- ✓ *S. aureus* decolonization
- ✓ **Selective digestive decontamination (SDD)**


Pérez-Granda MJ. et al. "Impact of selective digestive decontamination without systemic antibiotics in a Major Heart Surgery ICU (MHS-ICU)". National Congress of SEMICYUC. Oral presentation 19-22 June, Valencia, Spain 2016.

VAP episodes/1,000 days of MV

Before
16.26


After
6.80





Comité de Infecciones y Política de Antibióticos

RECOMENDACIONES SOBRE LA NEUMONÍA ASOCIADA A VENTILACIÓN MECÁNICA (NAV) EN ADULTOS



GRUPO DE APOYO A LA NEUMONÍA GRAVE (GANG)


Grupo multidisciplinar integrado por especialistas de distintos servicios para mejorar el manejo de la Neumonía Grave en la Institución (Extensiones telefónicas)

S ^a Microbiología Clínica	(78455/ 75001)
S ^a Medicina Intensiva	(78615)
S ^a Anestesia y Reanimación	(78888: REA / 78372: UCP)
S ^a Radiodiagnóstico	(78478)
S ^a Neumología	(78334)
S ^a Urgencias	(78506/ 78512)


AÑO 2015-2016

Descontaminación selectiva digestiva
(Se realizará a pacientes en que se prevea VM>48h hasta la extubación) y en el siguiente orden:

- Realizar higiene bucal con clorhexidina al 0,12% c/ 6 horas




- Extender la pasta oral (encías, paladar, lengua) con los dedos directamente o con una torunda / 6 horas (usar guantes).
En pacientes con traqueostomías: limpiar estoma con SF 0,9%, secar, aplicar clorhexidina acuosa y aplicar la pasta alrededor del estoma) cada 6 horas.



- Colistina 20 mg/g
- Nistatina 20 mg/g
- Tobramicina 30 mg/g
- Vancomicina 40 mg/g

- Administración de la solución digestiva:**
Combinación de antibióticos por vía digestiva cada 6 horas.
Al paciente que tenga SNG se le instilarán 10ml de la solución por la SNG, lavando la sonda antes y después con 20ml de agua.



Por cada 10ml de solución acuosa aromatizada:

- Colistina: 130 mg
- Tobramicina: 156 mg
- Nistatina 429 mg (2,6 mil UI)

La pasta oral y la solución digestiva se solicitarán a Farmacia.

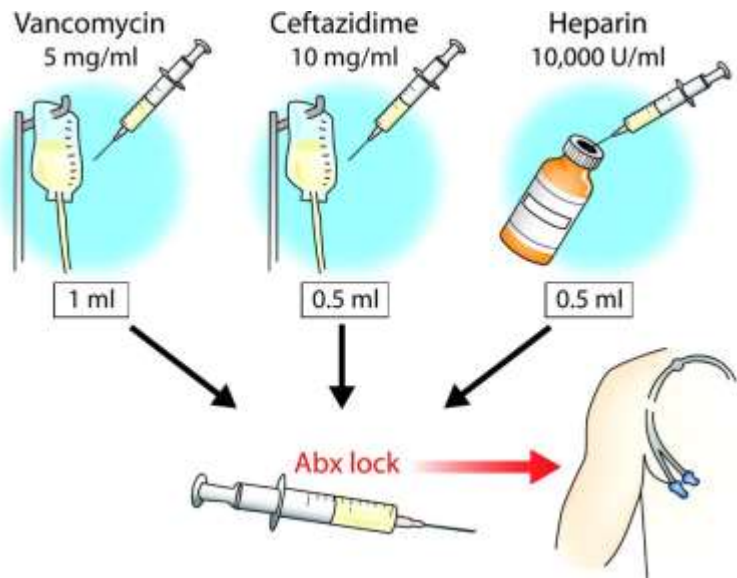
¹ Bouza et al. Chest 2008.

² Pérez-Granda MJ. Et al. J Hosp Infect 2013.

³ Dezfulian et al. Am J Med 2005.

⁴ Pneumatikos et al. Int Care Med 2002.

“LOCK THERAPY”



Catheter-related bloodstream infections



SDD subglottic space

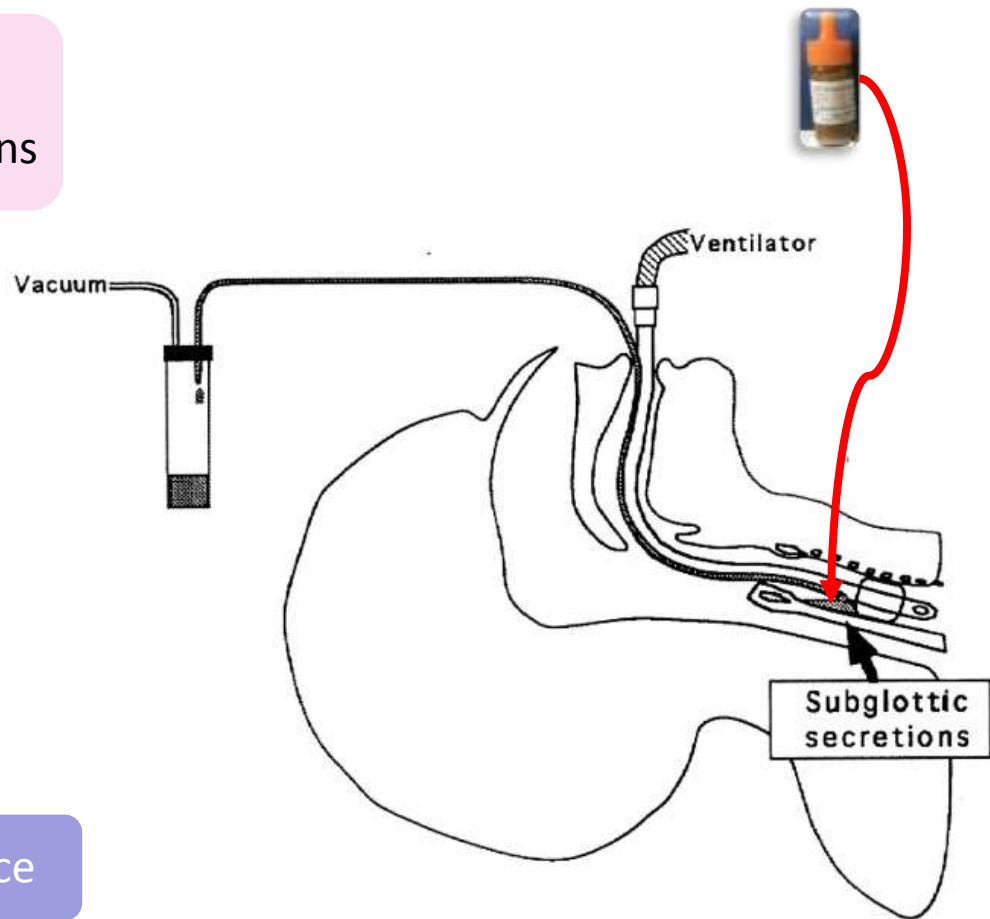


Image from the Clinical Journal of the American Society of Nephrology

HYPOTHESIS AND OBJECTIVE

HYPOTHESIS

The application of SDD solution as “**lock therapy**” in the subglottic space can reduce *P. aeruginosa* biofilm in ETTs.



OBJECTIVE

To apply an in vitro **bench-top model** to assess the efficacy of SDD solution applied in the subglottic space for eradication of *P. aeruginosa* biofilm in ETTs.

MATERIAL AND METHODS

3 ml 10^8 cfu/ml

72-h mature *P. aeruginosa** biofilm

composition of SDD solution

nystatin 2.6 mUI, tobramycin 15.6 mg/ml, colimycin 13 mg/ml

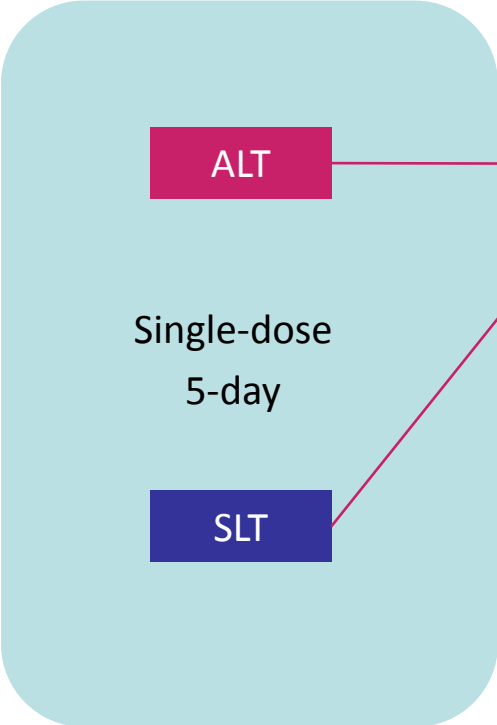


2-hour application of SDD or saline (+C)



Cuffed ETT (TapeGuard Oral Tracheal Tube Evac Murphy Eye, Mallinckrodt™)

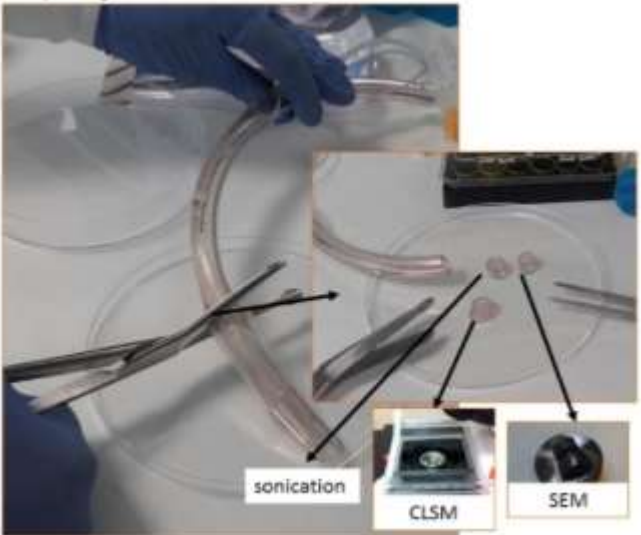
*ATCC 15442
Biofilm production was previously assessed using the crystal violet assay



All experiments were performed in triplicates.

Sonication of ETT segment { cfu/ml by culture
No. live/dead cells by CLSM

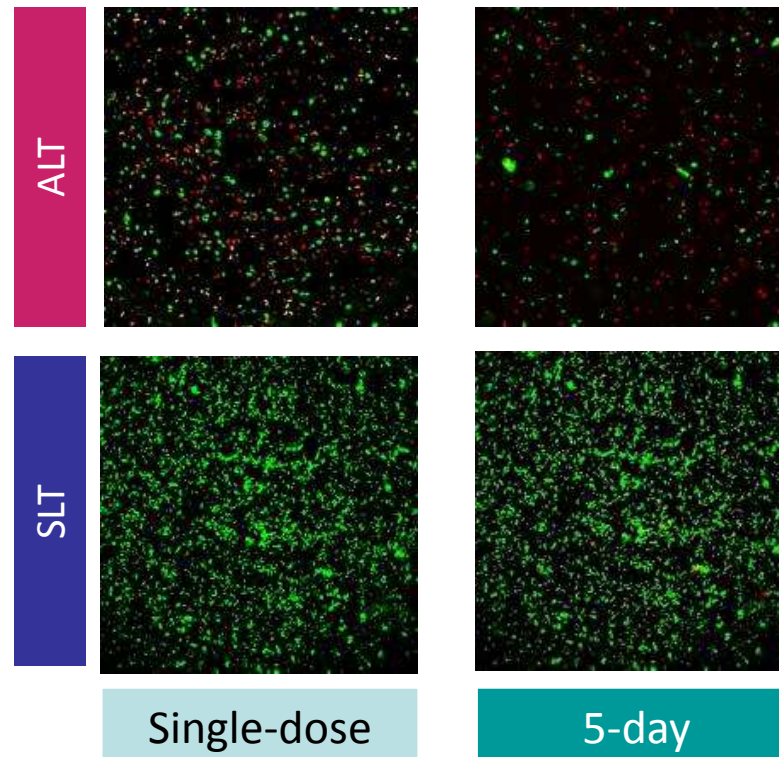
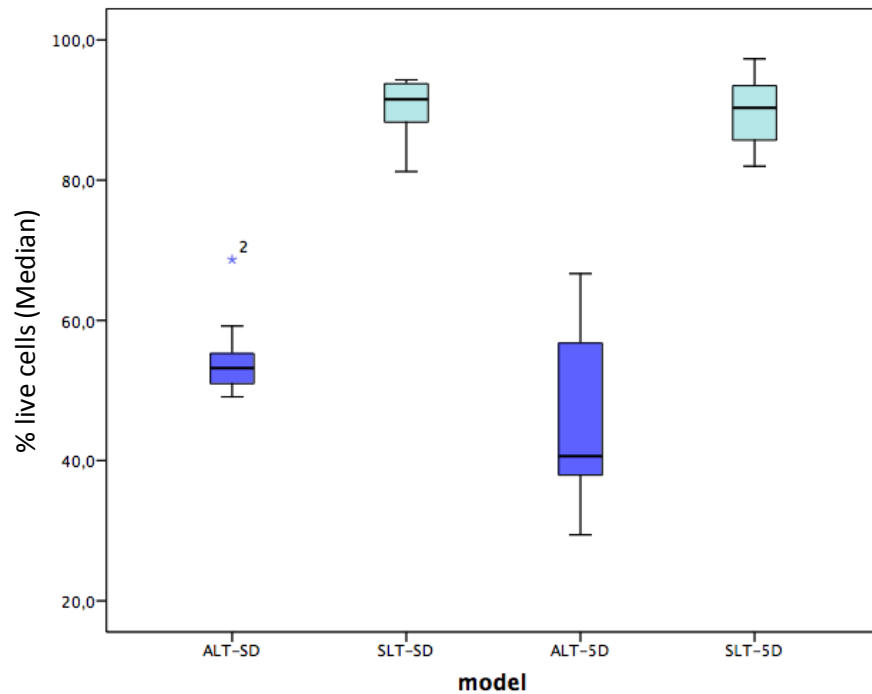
Visualization of ETT segments by CLSM and SEM



RESULTS

SONICATION OF ETT SEGMENT

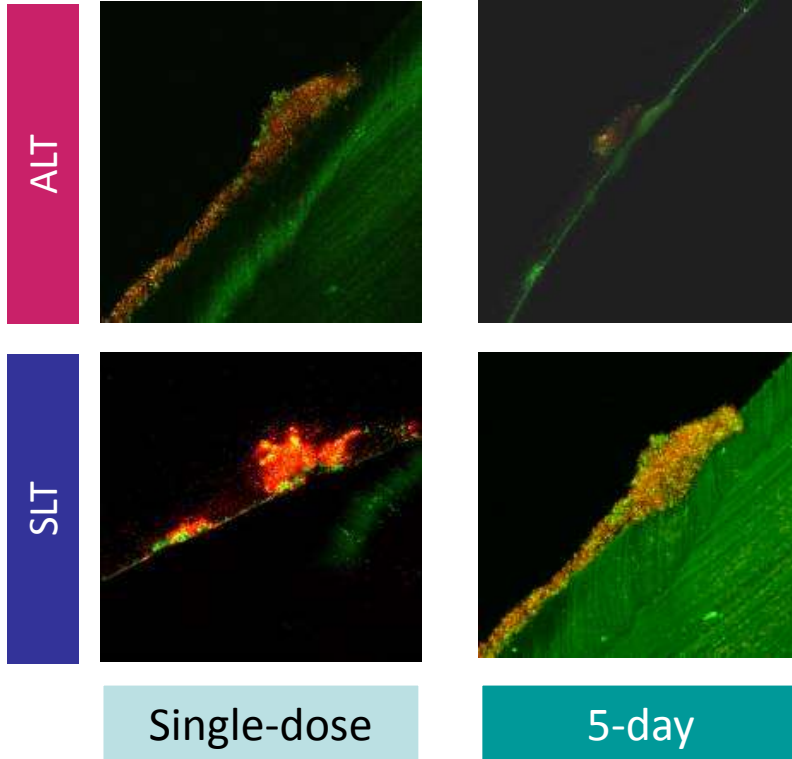
Variable	Lock Therapy					
	Single-dose			5-day		
	ALT	SLT	p	ALT	SLT	p
Median (IQR) cfu counts/ml	3.12x10 ⁵ (9.7x10 ⁴ -0)	8.16x10 ⁷ (7x10 ⁷ -0)	0.05	0 (0-0)	3.2x10 ⁷ (2.32x10 ⁷ -0)	0.03
Median (IQR) % live cells	53.2 (50.9-57.2)	91.5 (87.3-93.9)	<0.001	40.6 (36.6-60)	90.3 (84.8-93.9)	<0.001



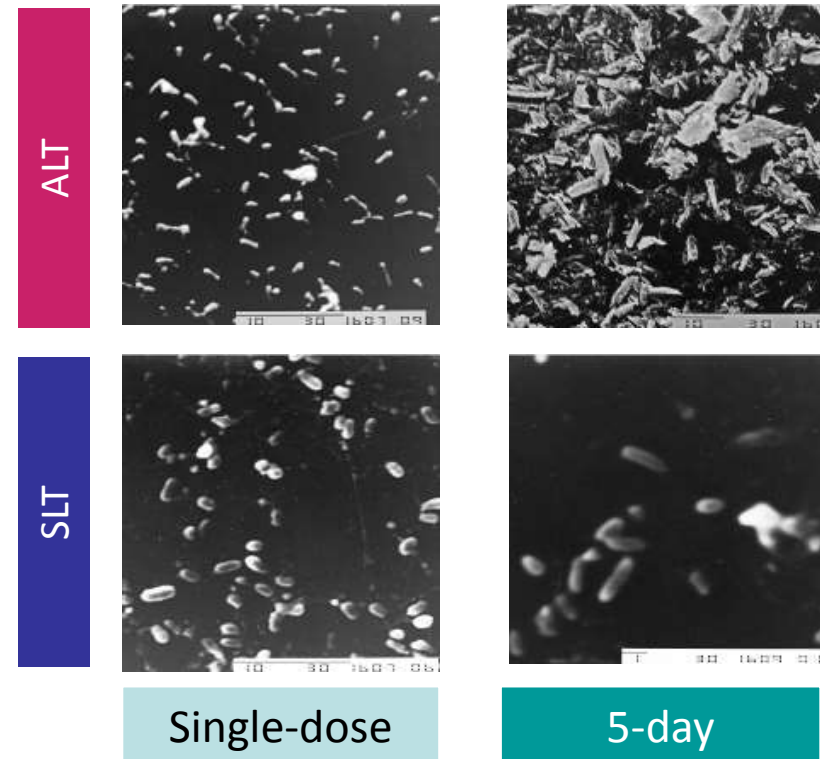
VBNC

RESULTS

VISUALIZATION OF BIOMASS



VISUALIZATION OF SESSILE CELL STRUCTURE



CONCLUSIONS

- ❖ Preliminary results: ALT with SDD solution significantly reduced 72-h biofilm of *P. aeruginosa* based on **culture and microscopy**
- ❖ Efficacy of ALT against biofilm of **other microorganisms** (prevention and therapy)
- ❖ Future studies: evaluate the efficacy of SDD solution as a **prophylactic measure** for VAP in patients under mechanical ventilation
- ❖ Our **bench-top model** = practical for **simulation** of colonization of ETT (diagnosis and therapy)

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