



Intrawound Vancomycin Achieves Sustained High Interstitial Concentrations in Injured Human Extremities

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Background

- **Intrawound vancomycin powder** may prevent biofilm formation and reduce surgical site infections
- **Systemic levels** of vancomycin after intrawound application in human subjects has not been thoroughly studied
- **Local levels** of intrawound vancomycin powder have not been characterized through **direct measurement techniques**



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Effect of Intrawound Vancomycin Powder in Operatively Treated High-risk Tibia Fractures A Randomized Clinical Trial

The Major Extremity Trauma Research Consortium (METRC)

- *JAMA Surgery* 2021
- Randomized clinical trial operatively treated tibial plateau or pilon fractures
- No effect on superficial site infection, bone non-union, or wound dehiscence
- Vancomycin powder **reduces gram-positive infections** by **3.4%** to **4.0%**



Systemic Absorption and Nephrotoxicity Associated With Topical Vancomycin Powder for Fracture Surgery

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- *Journal of Orthopaedic Trauma* 2021
- Prospective **observational** single site substudy of VANCO trial
- Assessed **systemic levels** and **nephrotoxicity**
- Serum vancomycin levels at 1 hour and **6-8 hours** after surgery
- None with detectable serum vancomycin levels, one increase in serum creatinine
- **Low clinical concern regarding toxicity** associated with systemic resorption

Purpose

Evaluate the pharmacokinetics of intrawound Vancomycin powder administered upon closure of open wounds associated with adult long bone fractures

Hypothesis:

Vancomycin powder will achieve **sustained intrawound levels** above the breakpoint MIC for MRSA ($1 \mu\text{g}/\text{mL}$) **without a significant increase in systemic levels** observed by a control



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Methods

Sampling technique: **Microdialysis**

- **Catheter- based** sampling method
- Collection of extracellular water-soluble molecules diffusing across a **semipermeable membrane** along a concentration gradient
- FDA cleared for intracranial use in humans Section **510(k) premarket notification #K102007***
- IRB approval (C.2020.056) obtained for adult open fractures

***All other uses are not FDA cleared and therefore in the USA may only be used with IRB approval or with an IDE from the FDA.**

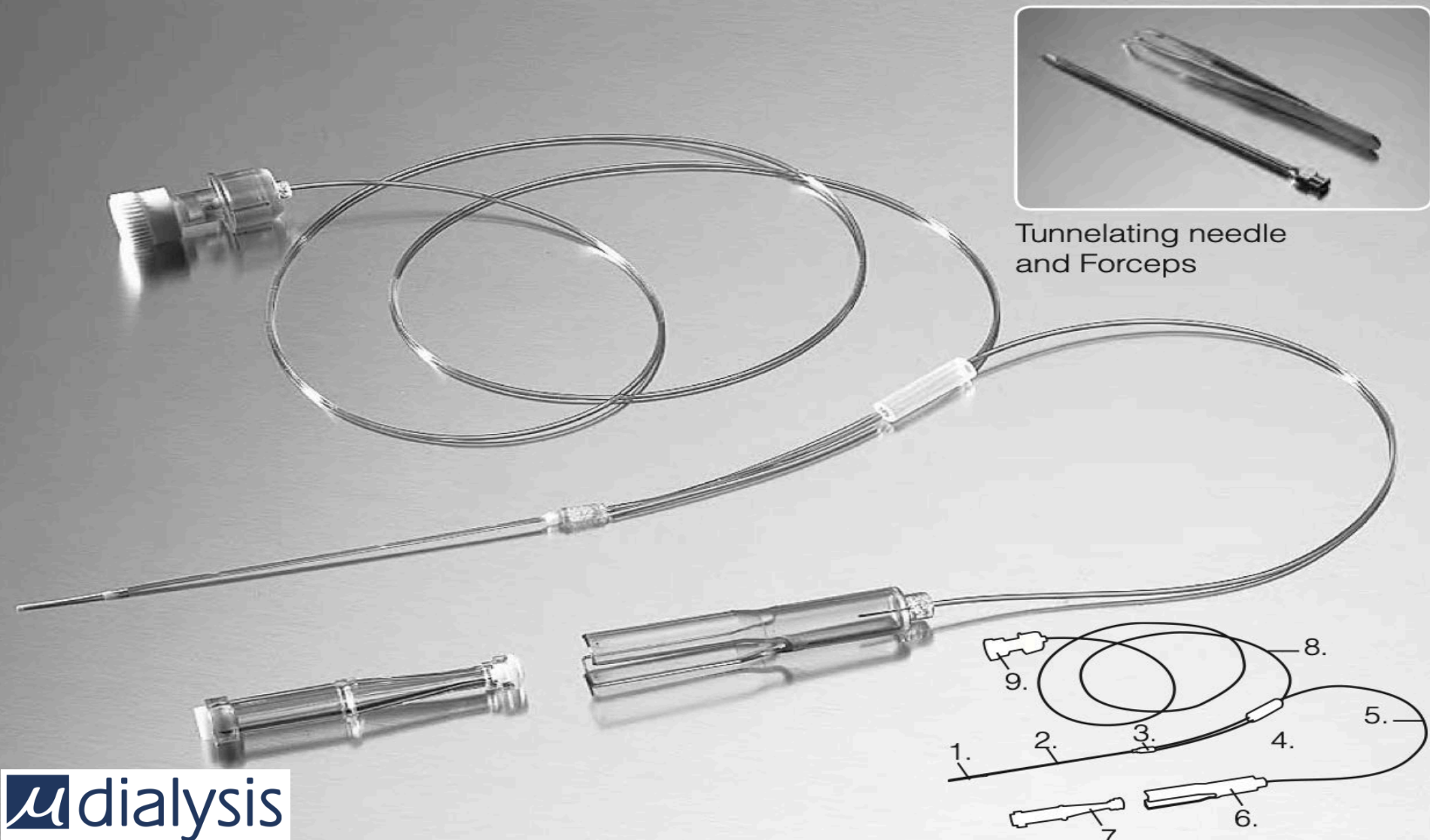


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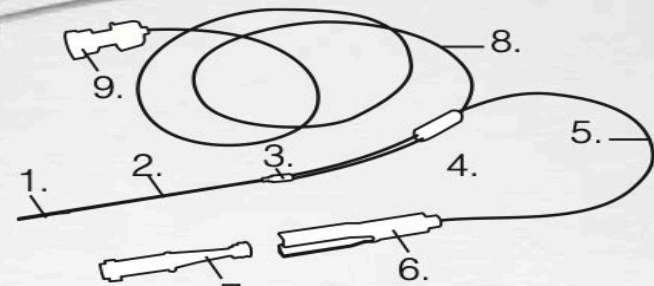


Methods

M Dialysis (Sweden) **CMA 70 brain MD catheter**, CMA 107 pump



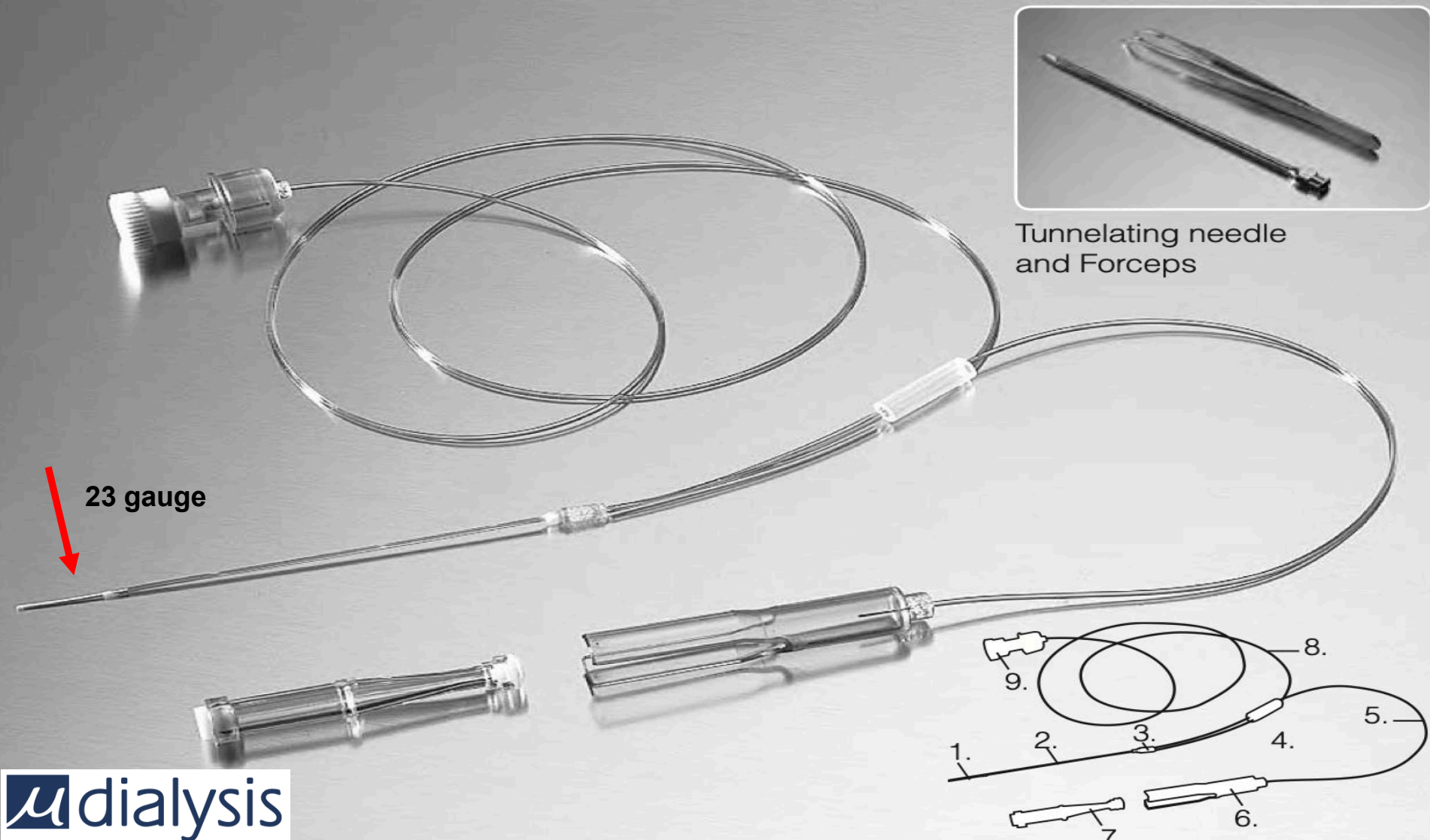
Tunneling needle and Forceps





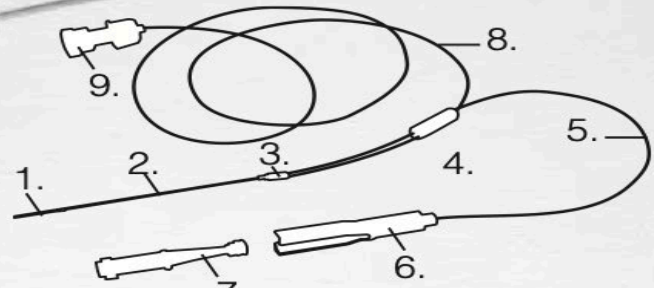
Methods

M Dialysis (Sweden) **CMA 70 brain MD catheter**, CMA 107 pump



Tunneling needle and Forceps

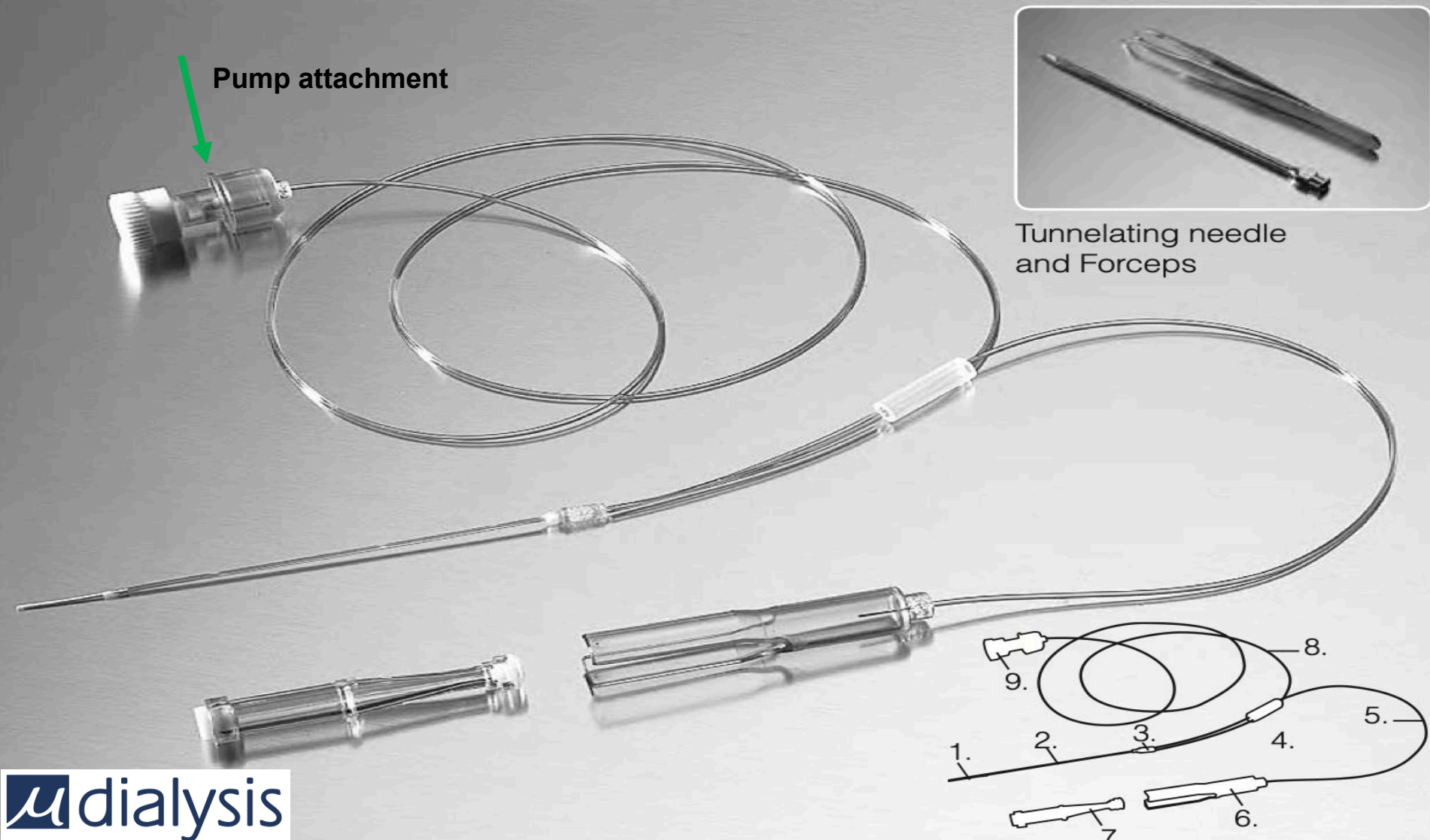
23 gauge





Methods

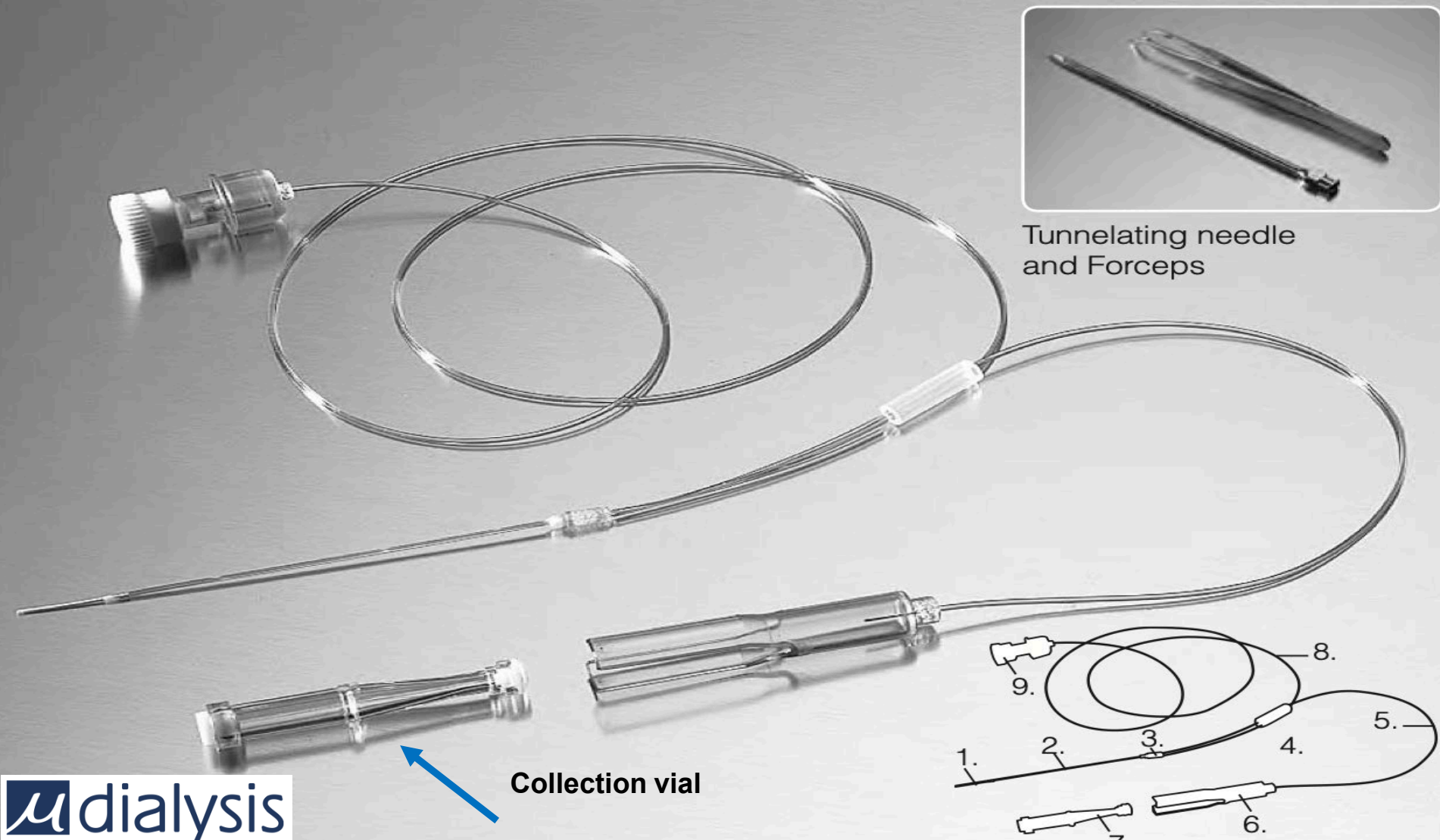
M Dialysis (Sweden) **CMA 70 brain MD catheter**, CMA 107 pump



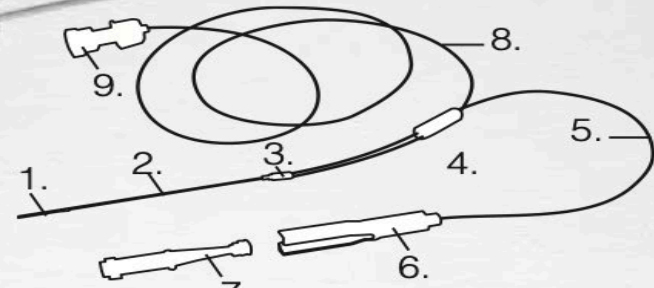


Methods

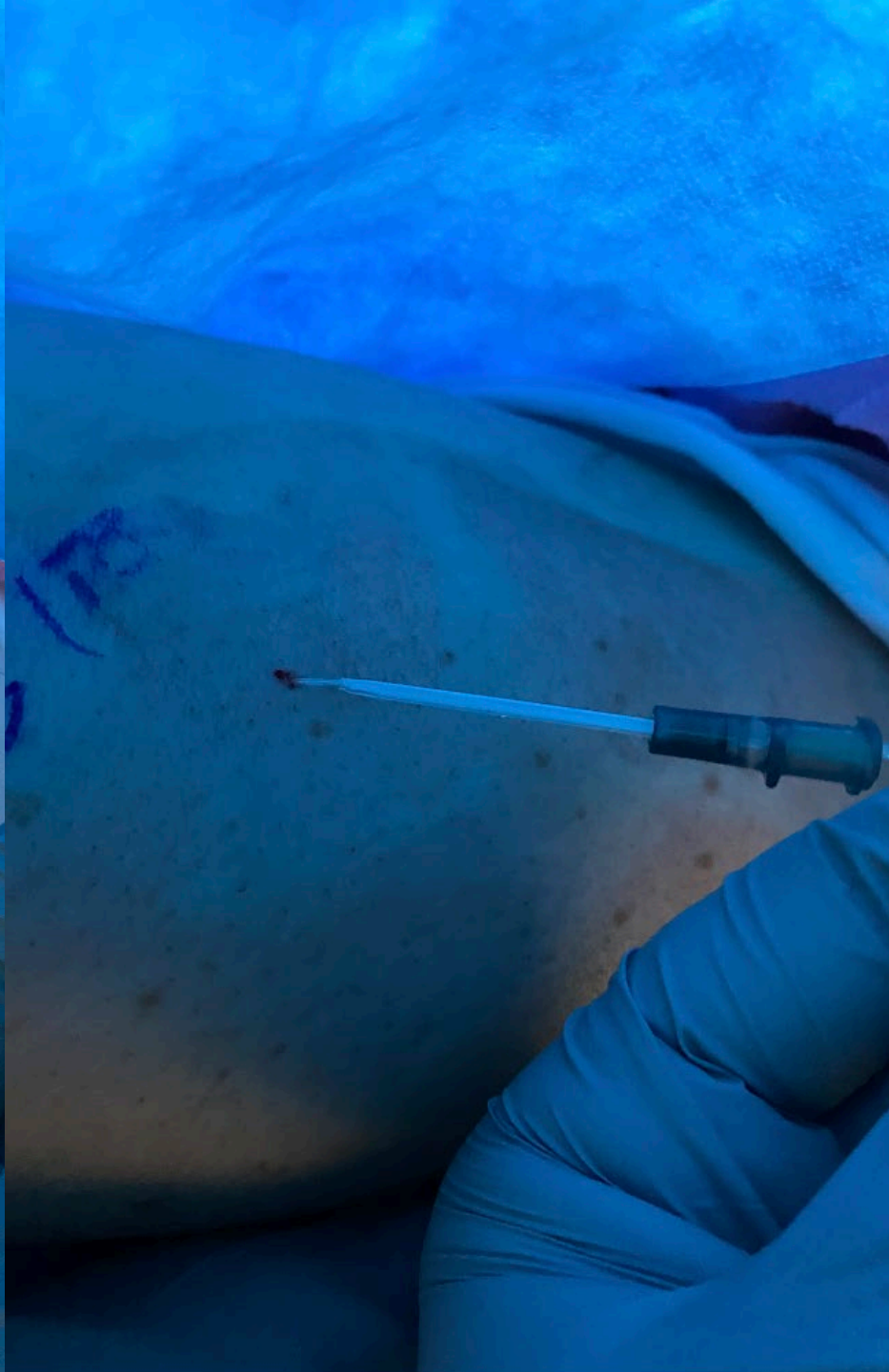
M Dialysis (Sweden) **CMA 70 brain MD catheter**, CMA 107 pump



Tunneling needle and Forceps



Collection vial

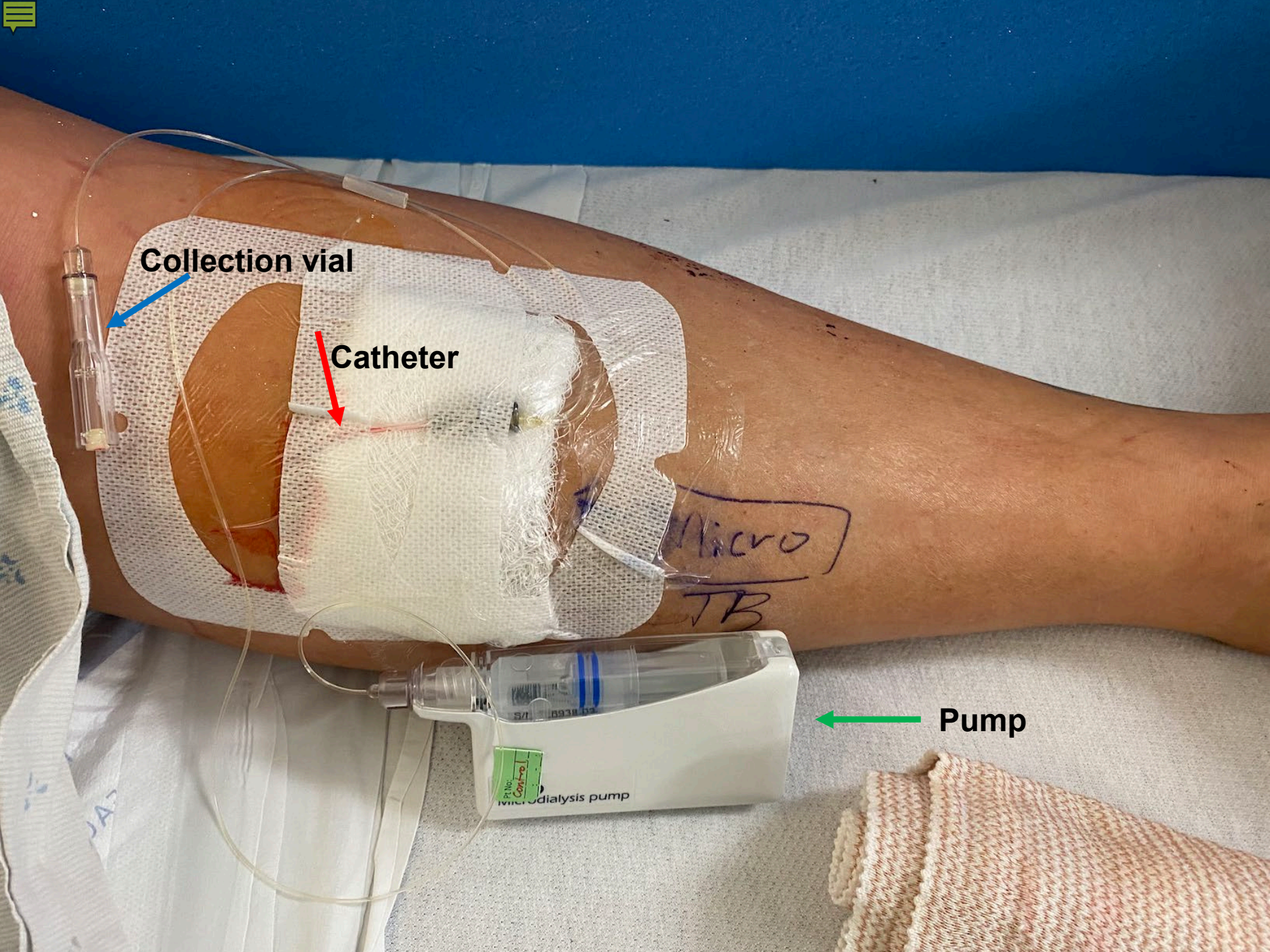


Collection vial

Catheter

Micro
TB

Pump



Methods

- Single center non-randomized **observational study**
- Adult patients with **open long bone fractures**
- Enrolled before initial OR debridement
- **1-2 g vancomycin powder** placed in wound bed



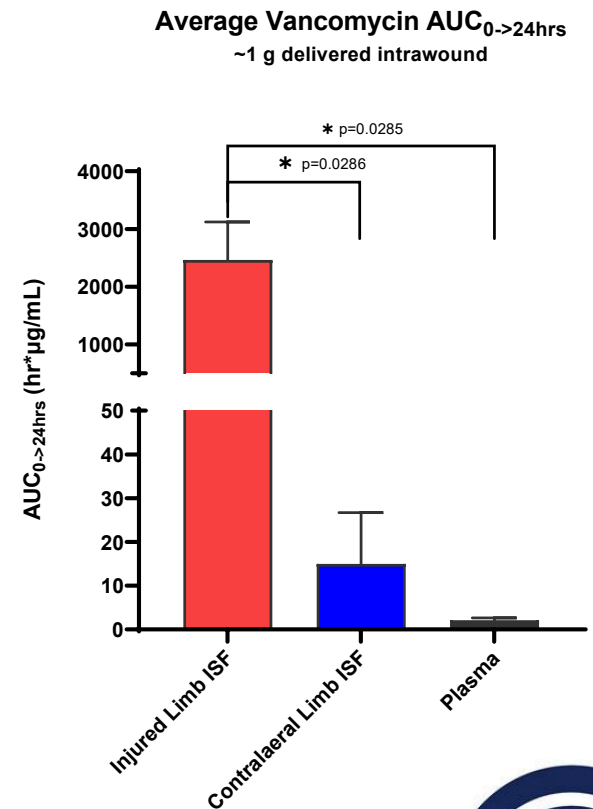
Methods

- MD catheter within **wound bed**
- Control catheter in **contralateral limb**
- Whole blood, dialysate samples obtained **24h**
- Free vancomycin in **plasma and interstitial fluid**
- **Ultra-high performance liquid chromatography**



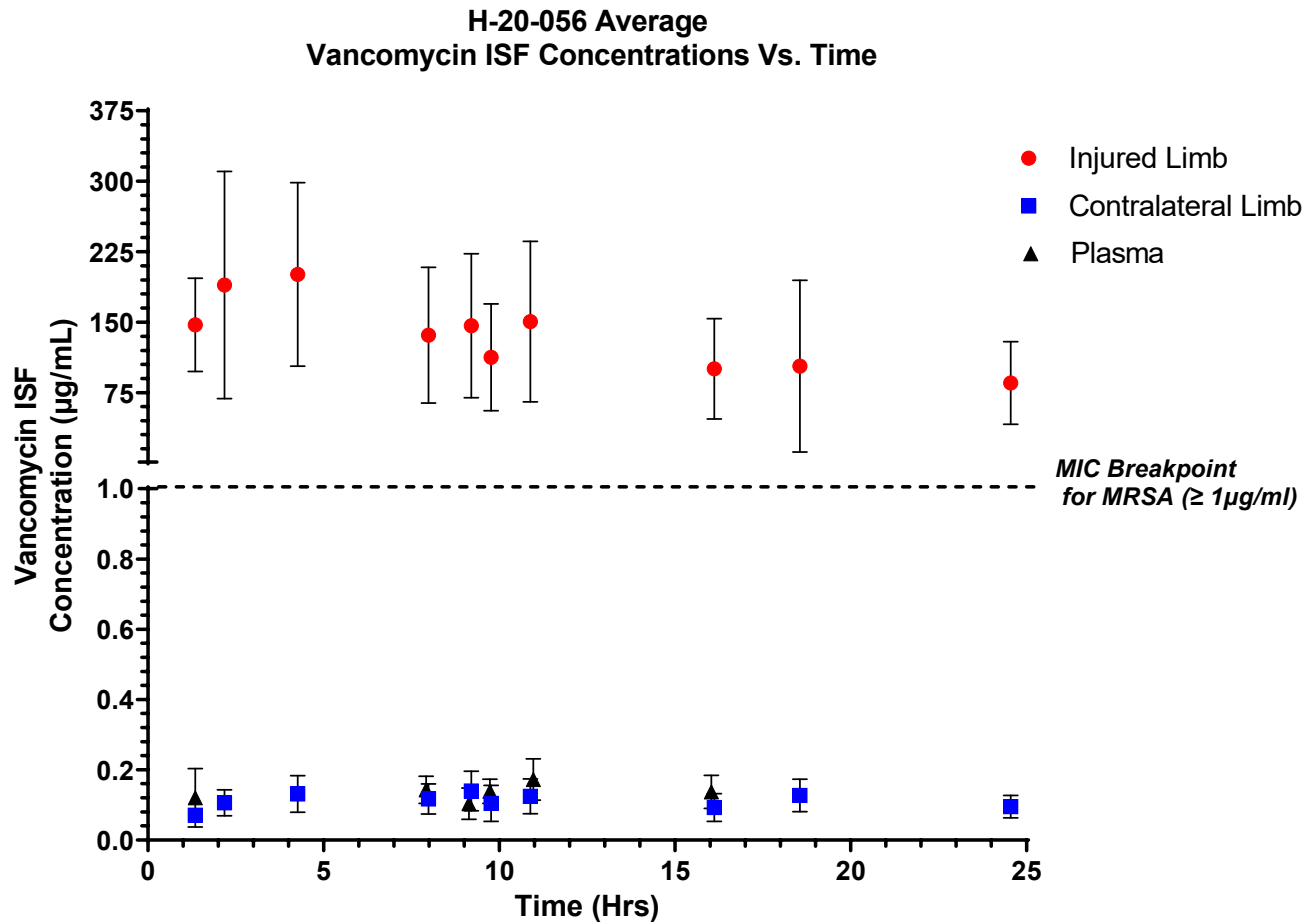
Results

- Five adult patients (1 female, 4 male; avg age 40yrs)
 - 4 tibia, 1 fibula
 - 3 GA type II
 - 2 GA type IIIA
- Avg C_{max} injured limbs 193.16 µg/mL
 - Avg 67.2% decrease over 24h
- Free Vancomycin exposure
 - Injured: 2463.46 hr·µg/mL
 - Uninjured: 15.00 hr·µg/mL
 - Plasma: 2.10 hr·µg/mL



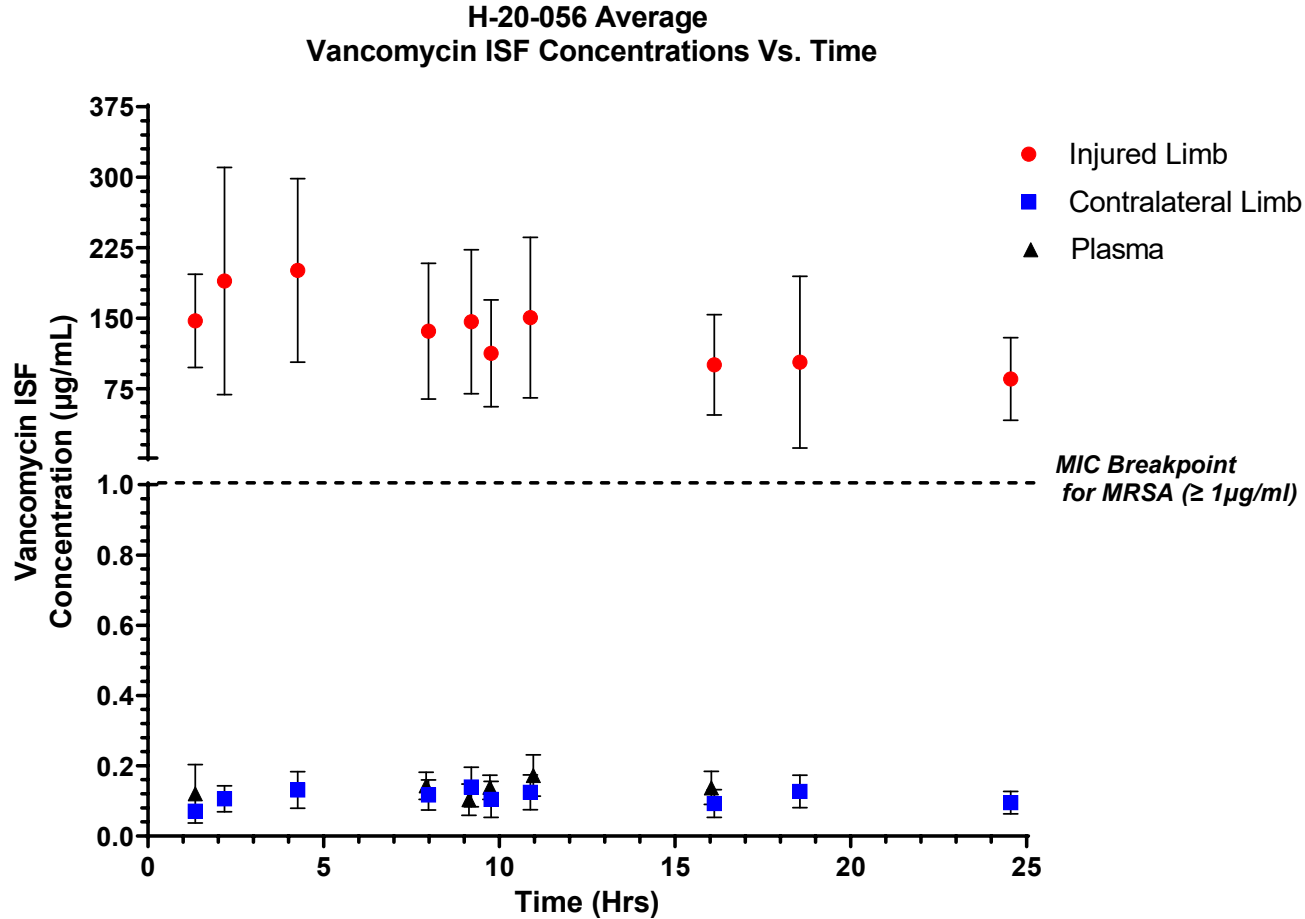
Results

Free Vancomycin levels **sustained above** ($>8 \mu\text{g}/\text{mL}$) **MIC for MRSA** ($1 \mu\text{g}/\text{mL}$)*



Results

Control and **Plasma** levels remained **below systemic toxicity** (<20-25 $\mu\text{g}/\text{mL}$)



Conclusion

1. First to **directly sample and characterize intrawound vancomycin** and compare to contralateral limb control using microdialysis
2. Free Vancomycin level remains above breakpoint MIC for MRSA
3. Concentration in **uninjured limbs** and **plasma** was **negligible**
4. Intrawound Vancomycin powder is **likely to remain effective and safe beyond 24 hours** if a therapeutic concentration is delivered

