# Sample Prep Module | NAATOS kickoff

Feb 14, 2024

# Agenda

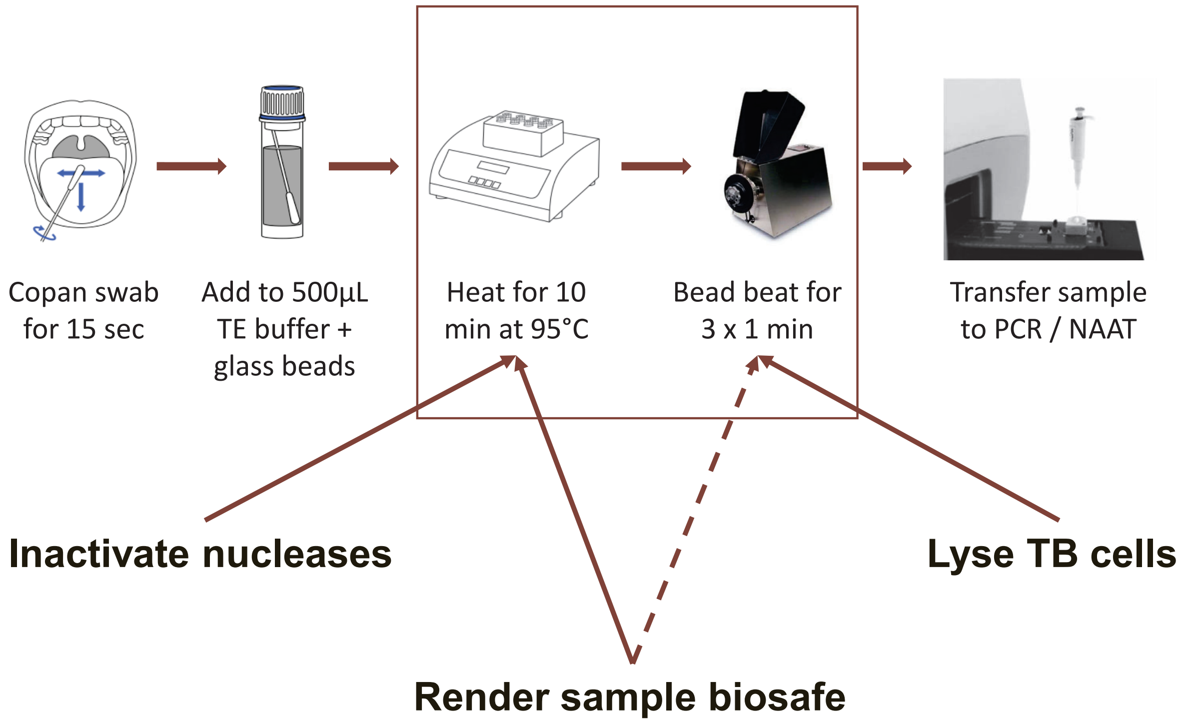
| | |
|---|---|
| Intros | All |
| Overview / how we got here | Matt K |
| Deeper look at specs | Matt K |
| Current design details | Bryan N |
| Plan moving forward | All |

# Overview, or how did we get here

# Many alternative TB testing methods, tongue swab is the best

| # | Category | Specimen | Benefits of testing method | Limitations |
|---|---|---|---|---|
| 1 | Current Method | Sputum | • Used for 140 years to diagnose TB<br>• Can usually be obtained from patients with respiratory symptoms, given enough time/effort<br>• Usable for diagnosis, treatment monitoring, and DST<br>• Current DST ecosystem designed around sputum | • Unwelcome & stigmatized<br>• Difficult to obtain in children, PLHIV, elderly, and in systematic screening<br>• Occupational hazard for HCW<br>• Viscous, heterogenous, poorly reproducible, difficult to process |
| 2 | Alternative Respiratory-based testing methods | Tongue Swab | • The world just got swabbed; scalable<br>• TB is recoverable from tongue swabs with good concordance with sputum results<br>• Tongue swab eluent offers highly-simplified specimen processing, relative to sputum<br>• Highly stable specimen, even at elevated temps | • Less sensitive for very low bacillary loads |
| 3 | | Cough | | |
| 4 | | Saliva | • Easy to test | • Larger volume required<br>• Dilute sample |
| 5 | | Breath | • Easy to test | • Early stages of product development, still unclear what results mean |
| 6 | Alternative Non-respiratory based methods | LAM | • Simplified sampling, compared to sputum<br>• May have extrapulmonary TB Dx advantages<br>• Low cost | • Suboptimal diagnostic accuracy (LAM) |
| 7 | | Stool (peds)<br>Host RNA<br>Cell-free NA | • Simplified sampling, compared to sputum<br>• Enables sampling of pediatric populations<br>• May be able to diagnose subclinical disease | • Complicated sample handling (stool)<br>• Early stages of specimen characterization (RNA and cfDNA)<br>• Complicated processing (RNA, cell-free) |

# Current tongue swab consortium “standard” sample prep accomplishes 3 primary tasks we need to translate for POC



# The fortified TB envelope complicates approaches to lysis

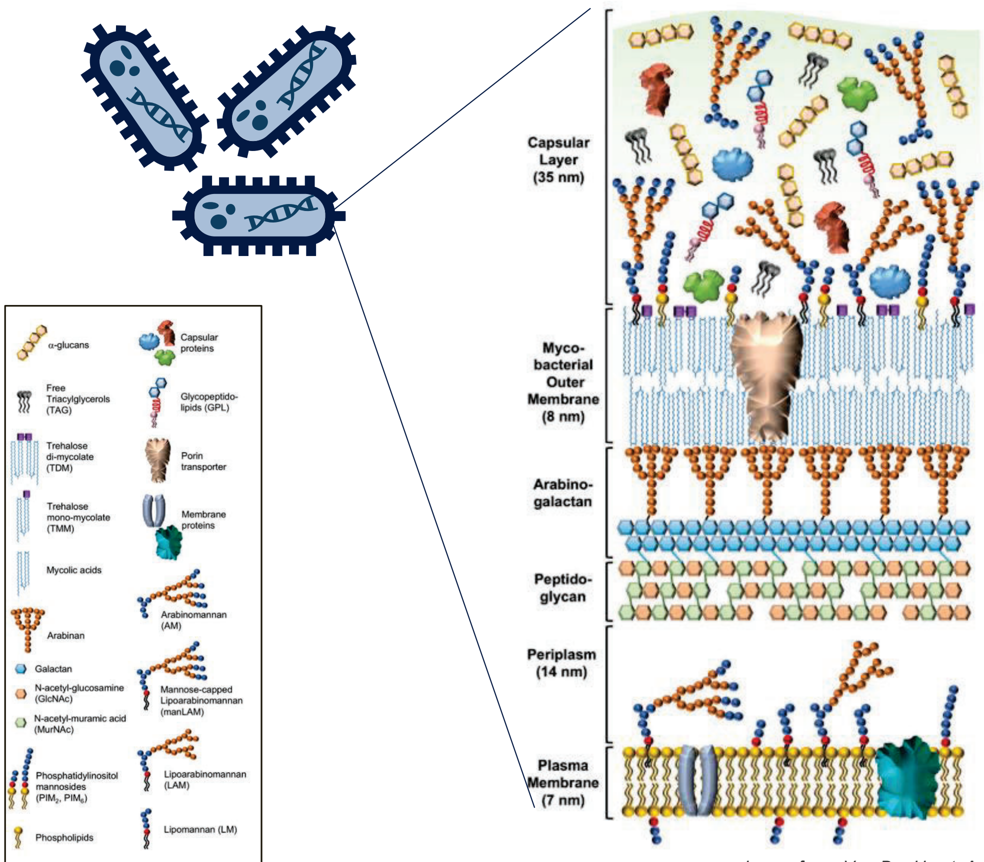
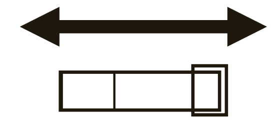



*Image from: Van Der Horst. Analyst. 2021.*

# Current lysis approach characteristics and limitations informed the design space for novel mechanical BB solutions at POC



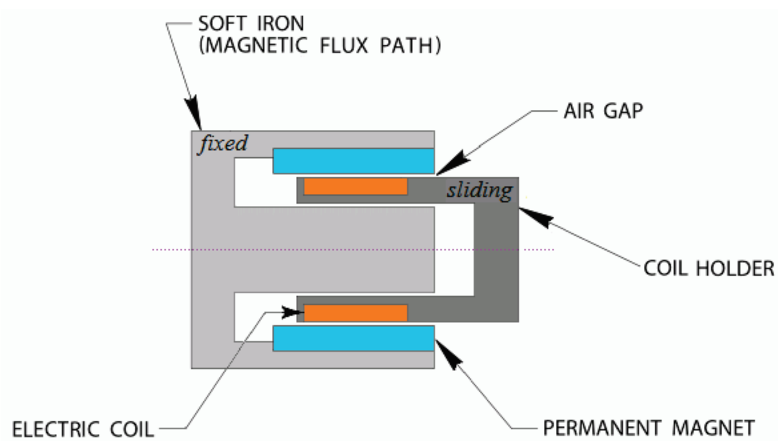


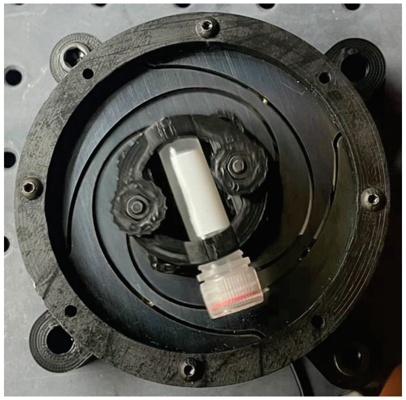


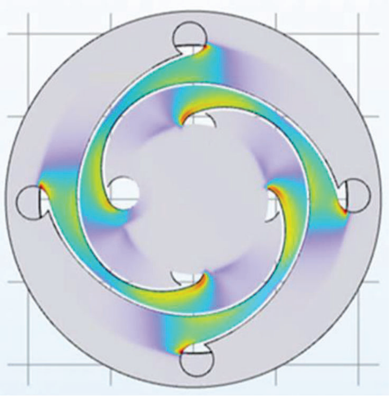
| | Biospec Mini-Beadbeater | Vortexer + Adapter | SoniBeast Jr | Lego hand-crank | Hand-shaking |
|---|---|---|---|---|---|
| Energy Requirement | Electrical Power | | | No Electrical Required | |
| Oscillation frequency (Hz) | 58 | 50 | 300 | 10-15 | 2-3 |
| Throw / displacement (mm) | 19 | 4+ | 2.5 | 25 | >100 |
| Motion profile | Figure 8 | Circle | Linear oscillation | Elliptical | Hammer-like |
| Power source | Mains | Mains | Lithium battery | Manual | Manual |
| Power draw (W) | 850 | 135 | 50 | N/A | N/A |
| Time for optimal result (min) | 3 x 1 | 5 | 2 | Not possible | >5* |
| User experience | Walkaway | Walkaway | Uncomfortable | Variable / tiring | Variable / tiring |
| Price ($) | 2500 | 600 | 320 | 10 | 0 |

# Why we focused on voice coils for internal development

- Considered many ways to shake a tube within bounds of previous slide, and settled on voice coils as a cheap, rugged technology both to study key motion parameters and potentially become a product
- Relative to many other mechanical means, voice coils offer:
  - High efficiency due to their harmonic nature, which allows linear motion without the need for constant acceleration and deceleration of the load
  - No contact wear or friction given their structure, which also minimizes unwanted vibrations / sounds
  - Extreme longevity without maintenance given the above and the long history of commodity-level production
- Primary challenge to overcome for use of voice coils was adapting the flexure plate to support the relatively larger displacements needed for lysis compared with, e.g. vibrating a speaker cone



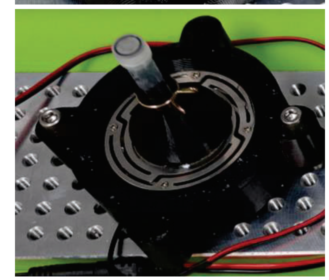



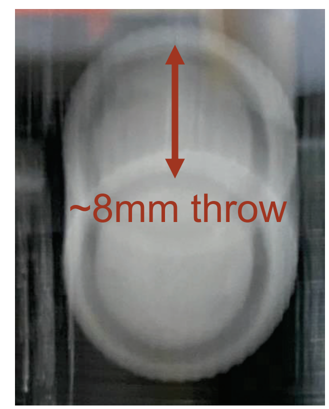


# Several key learnings stemmed from initial voice coil work

- General experimental notes:
  - All results noted here used TB-spiked oral matrix (from volunteer tongue swabs) and 150mg of 100μm glass beads in the sample tube
  - Lysis efficiency (%) calculated relative to the copies/mL PCR output from the TB tongue swab reference assay of 10 minutes at 95C and bead beating in the BioSpec mini bead beater

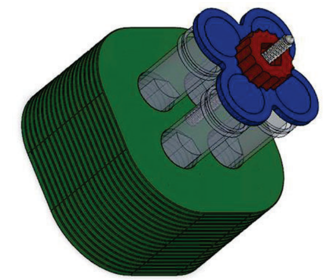
- Lysis was dramatically more efficient when shaking perpendicular to the tube’s long axis compared to parallel
- Orienting the tube horizontally vs. vertically (upright) did not have any notable effects
- Leaving the swab tip in the tube equaled or improved lysis efficiency vs. no swab tip
- Bead type, size, and amount maintained their parameter values from previous optimization for use in other mechanical bead beating systems
- Initially performed the bead beating after letting samples cool to room temp following 10 minutes at 95C
  - In this condition, optimal lysis efficiency required 8-9 mm displacement, or throw
  - Frequency had a smaller effect than throw, with sufficient performance in the 70-110 Hz range



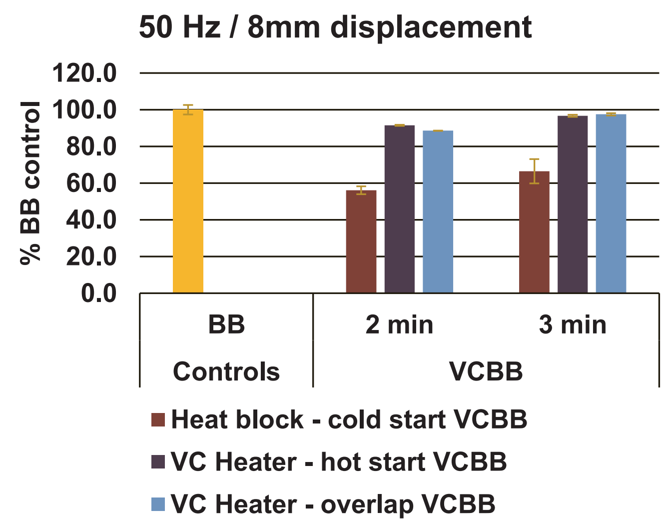


# Lysis becomes easier with integrated heater

- Initial experiment showed ~10% lysis efficiency improvement when putting samples directly into voice coil setup from the heat block
- Devised new architecture to integrate the heater into the voice coil tube holder
  - Both the heater and tube holder are constructed from a stack of printed circuit boards (PCBs)
  - Double duty keeps the heater/tube holder cheap and light
  - Found we can heat and shake 4 tubes at once using a single voice coil / flexure plate



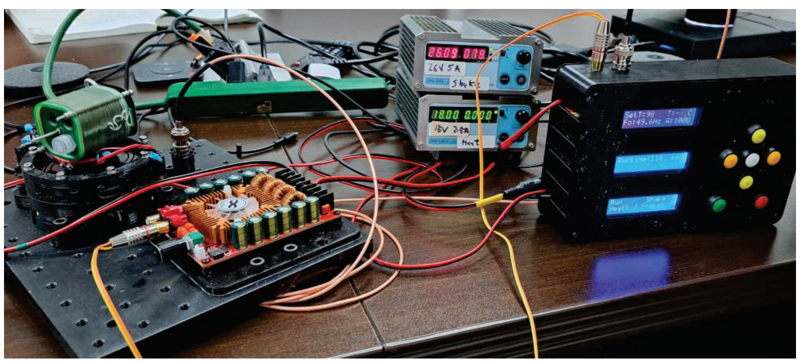
- New integrated design showed substantially higher lysis efficiency compared with bead beating room temp samples (fig on right)
  - No significant differences between leaving heater on during shaking and turning off heater just before shaking
  - PCB heater/tube holder insulates tubes well against heat loss
- Integrated heater allowed for smaller displacements (~7mm) and lower frequencies (50-70Hz) to achieve optimal lysis efficiency
- Subsequent optimizations of temperature, heating duration, and bead beating duration for lysis efficiency, nuclease inhibition, and biosafety led to the “final” protocol on following slide



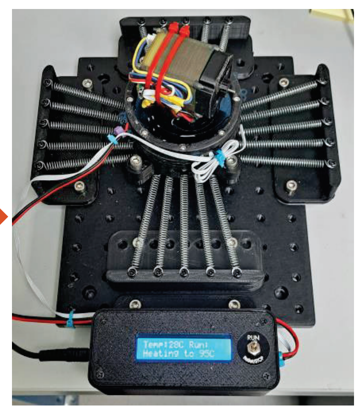
# Current Design Approach | Reusable Lysis Module

- Current plan to meet product requirements is our voice coil bead beater (VCBB) with integrated heating
  - Lysis performance at least on par with “gold standard” heat plus BioSpec bead beating (detailed on next slide)
  - Run time of 6-7 minutes for 1-4 tubes at a time
    - Temp ramps to 95C in ~1-2 minutes, depending on starting condition
    - Temp holds at 95C for 2 minutes, then heater turns off
    - Voice coil bead beating lasts for 4 minutes, sample remains hot during that time to aid lysis performance
  - Projected BOM < $100 at moderate scale of quantity 1000
  - Minimal power draw to enable easy battery operation
- Prototypes have gone through several iterations, will soon undergo external DfM and productization

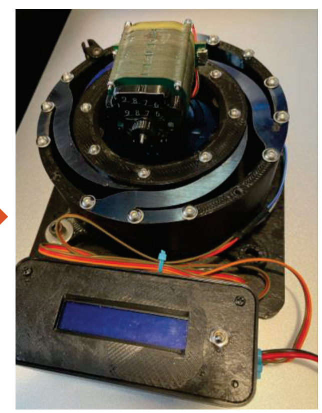
**First heat-integrated lab version**



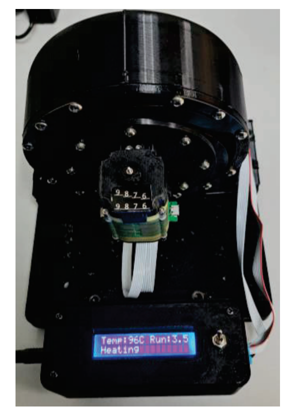
**Uganda study (R1)**



**Further lab studies (R2)**

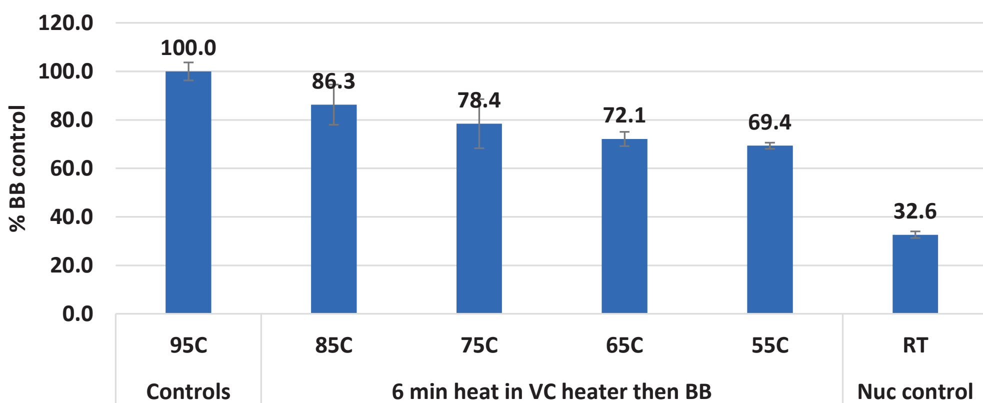


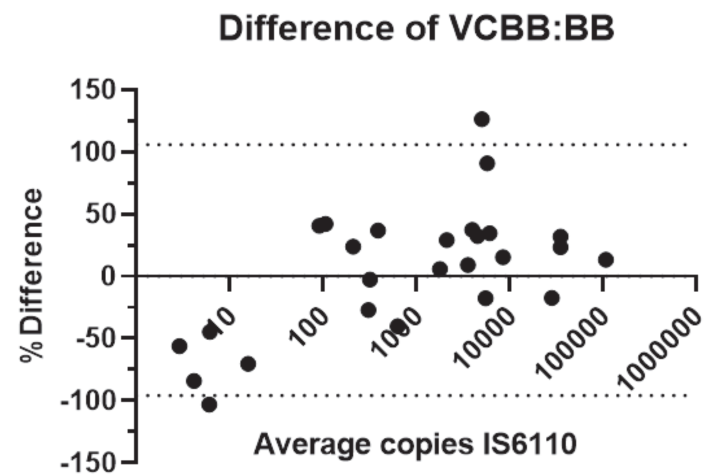
**Final GHL rev (R3)**



# VCBB has demonstrated performance in line with reference assays

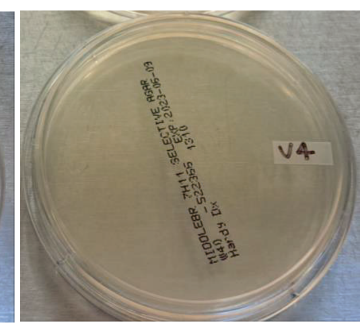
- Uganda R2D2 site study with patient samples confirmed previous findings for VCBB R1 with contrived samples
  - VCBB R1 typically outperformed BioSpec BB, except at very low copy numbers (Rev3 design alleviates this issue)
- Lysis efficiency is maintained for temps down to 65C, but nuclease inactivation is not as effective at lower temp
  - Tested by letting samples sit at room temp for 60 mins following integrated heat and lysis, before PCR




- Using the Uganda study unit and protocol, biosafety experiments showed 0 colonies at 8 weeks

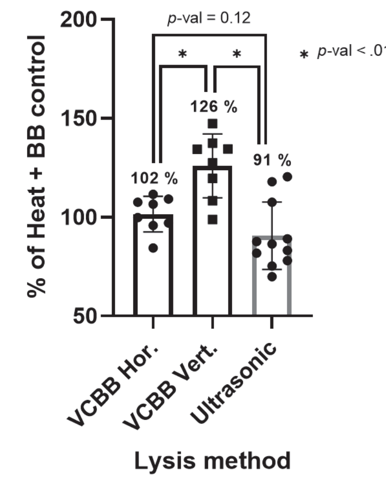
No treatment




VCBB

# Continuing to support and monitor other sonication sample prep approaches

- Performed explorations with an ultrasonic horn OEM dev kit
  - Very similar to what is used in GeneXpert
  - Explored lysis efficiency as function of:
    - Ultrasonic horn amplitude
    - Clamping force
    - Tube material
    - Duration (total and per cycle)
    - Presence and amount of beads

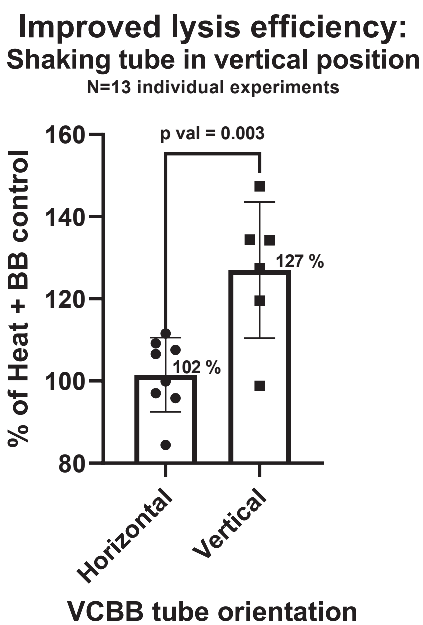


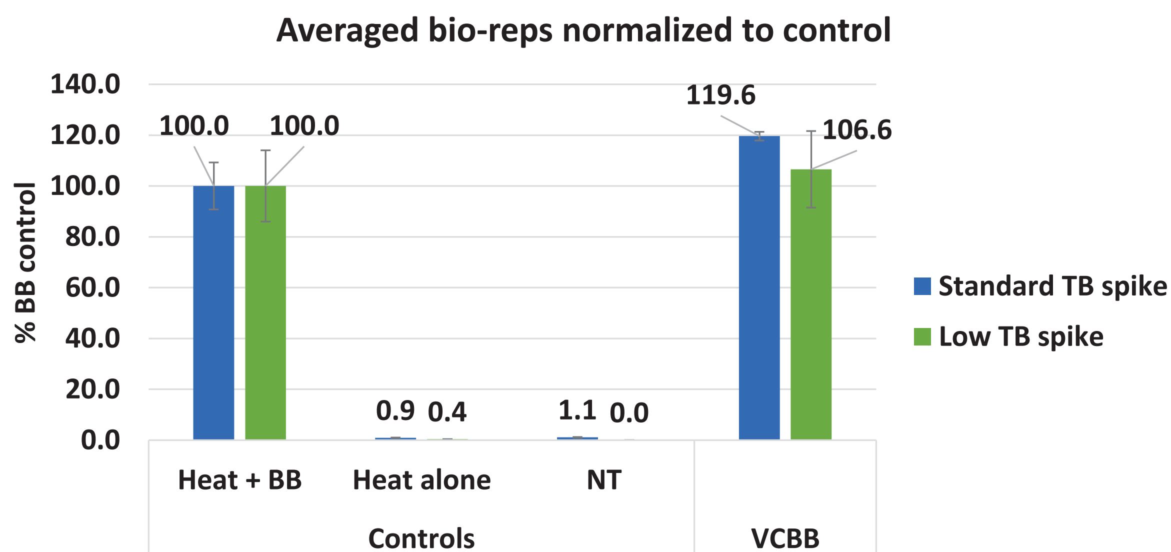

- Discovered that conditions we found to be optimal were very similar to a collaborating company
  - Two cycles of 30s with 30s off between, include glass beads, draw ~12-15 W of electrical power
  - Side by side testing showed nearly comparable efficiency (vs. VCBB Rev1), nuclease inactivation, and biosafety; VCBB Rev3 now outperforming ultrasonic
- For processing 4 sample tubes, ultrasonic and VCBB use about the same total energy and time, but US is 1 at a time, vs. 4 at a time for VCBB
- Primary reasons for using VCBB for NAATOS are performance and cost, as US BOM is still > $500
- Will continue to monitor price-lowering efforts and freely share our US lysis knowledge generated

# Further look at key requirements / specs

# Vertical (upright) tube orientation is required

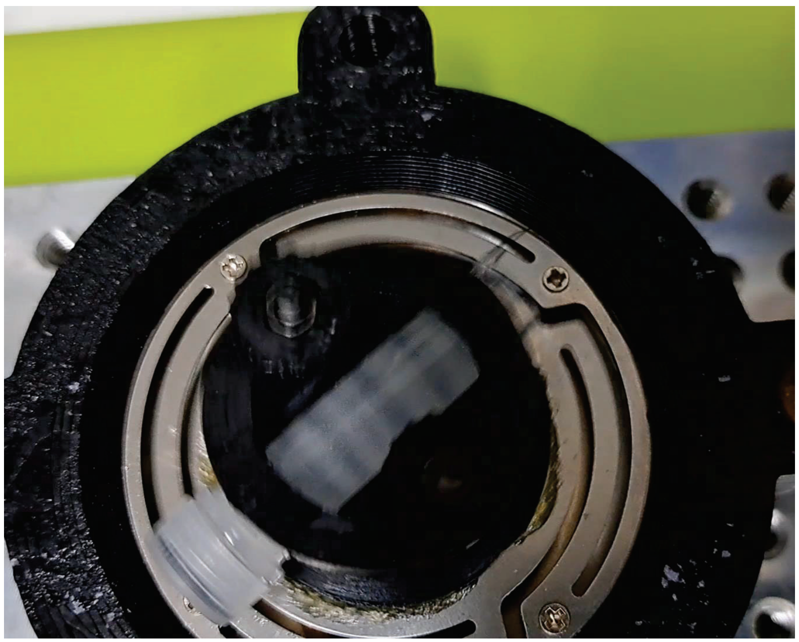
- Recent designs with upright tube orientation have shown consistently superior results to horizontal tube configurations, including at low copy numbers
- Allows for smaller heater area/volume with liquid collected at bottom of tube

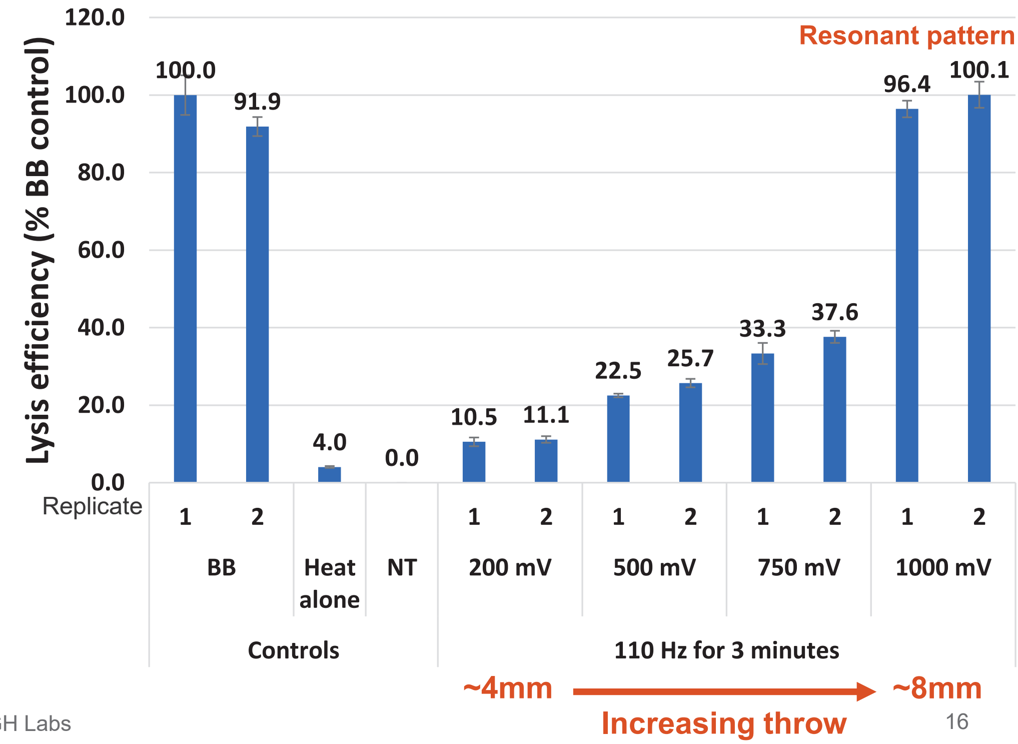


# All else constant, throw appears to have the largest impact on lysis efficiency

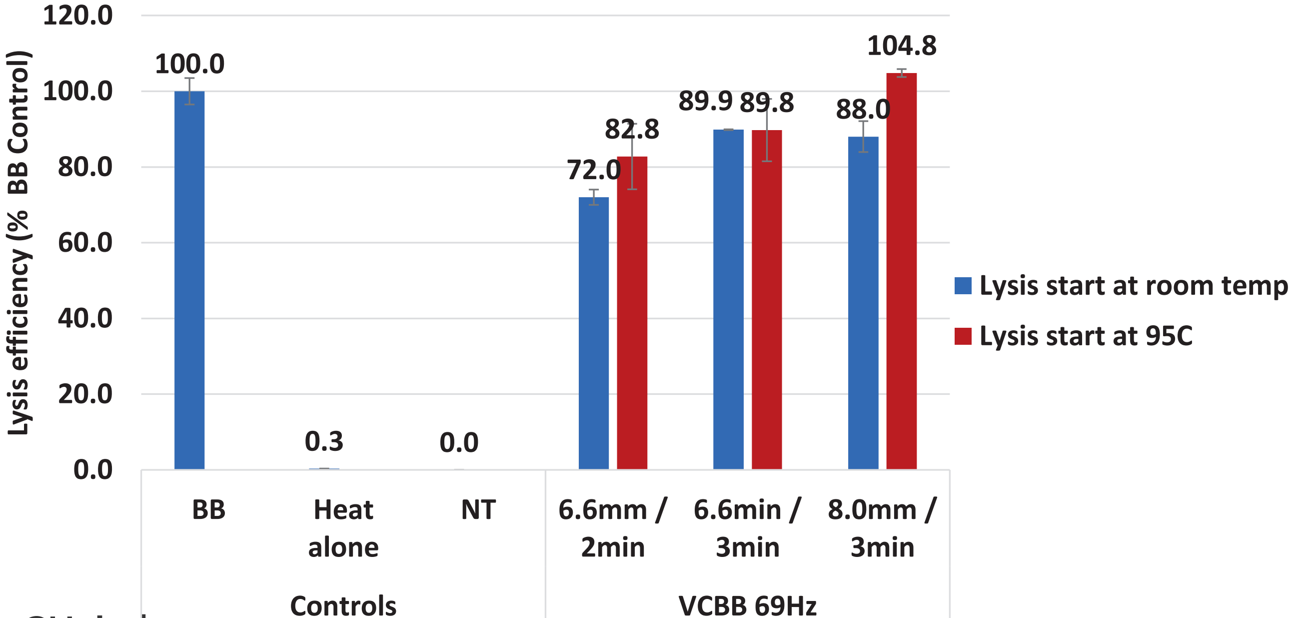
- With integrated heating, current best spec for throw is 7 +/- 0.5mm
- Will perform additional tolerance testing with current design in coming weeks





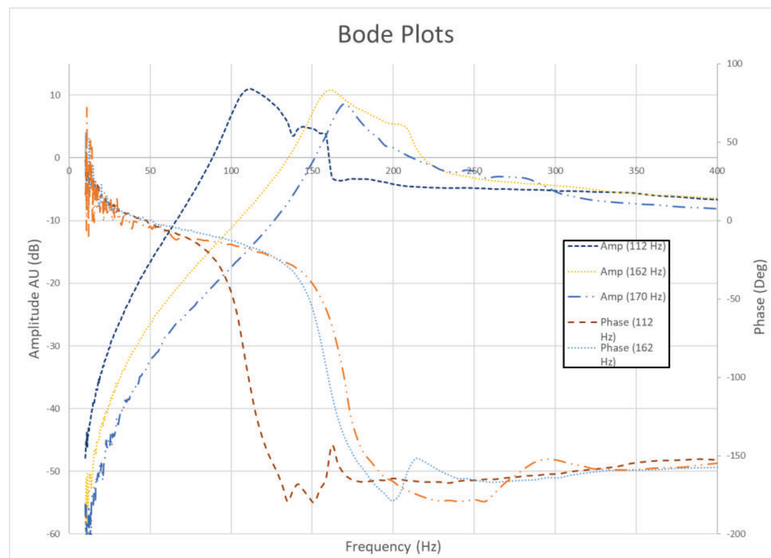
# Hot start (but not integrated heating) experiment showed fairly comparable results for 6.5 to 8 mm throw

- Non-heated lysis experiments required throw >8mm for best efficiency
- We turned throw up to 11 (mm) one time, but results were predictable given the *Spinal Tap* reference
- This hot start experiment showed modest improvement from 6.5mm to 8mm
- Rev3 design has 7mm throw, which has worked consistently well for integrated heating versions



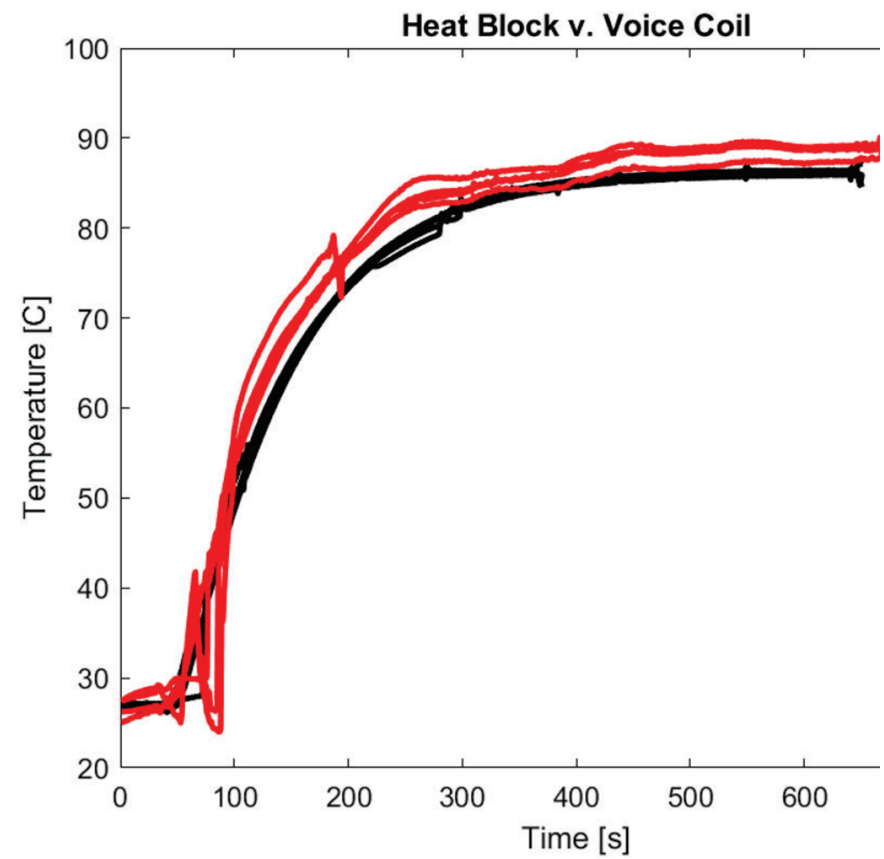
# Oscillation frequency has a smaller effect

- Current best spec with integrated heating is 65 +/- TBD Hz
  - From a lysis efficiency perspective, tolerance is likely around +/- 5 Hz
  - From a production / efficiency perspective, tolerance more likely +/- 1 or 2 Hz
- Previous testing largely a result of designing different flexure plates with lower or higher resonant frequencies, ranging from 50 to 110 Hz
- Want to minimize power draw via lower frequencies, but still need some minimum value for a given throw and time regime, which have larger impacts
- No commercial devices for lysis use < 50 Hz



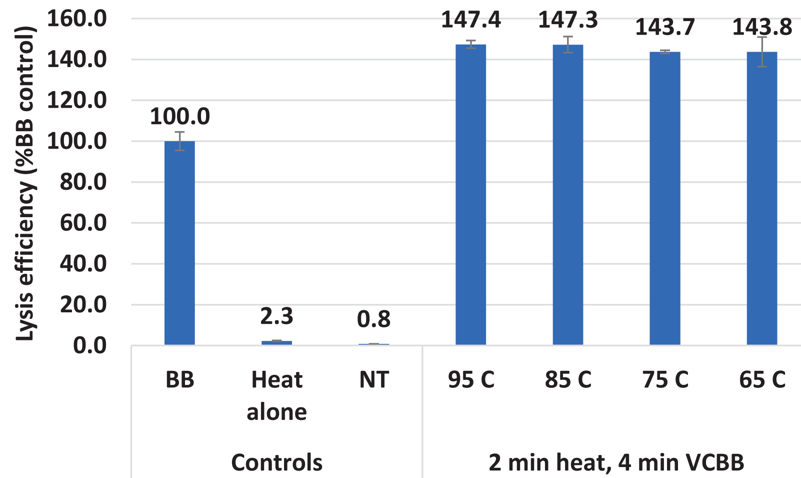
# Heating temp tolerance is moderate

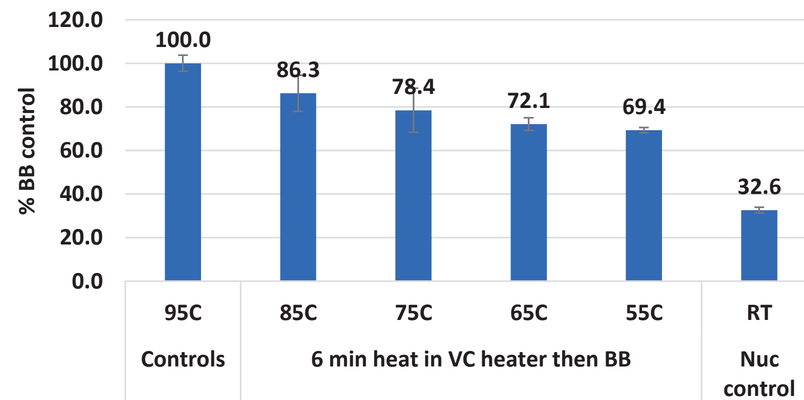
- Current best spec is 95 +/- 3C at the heater/tube interface, assuming a 3-5C differential between tube exterior and liquid
- Basically want to get all the liquid to 90C without boiling it
- Plot to right shows thermocouple traces immersed in a sample tube inserted in VCBB heater (red traces) vs. an aluminum heat block (black traces), both nominally at 95C



# Heating temp driven more by nucleases than lysis

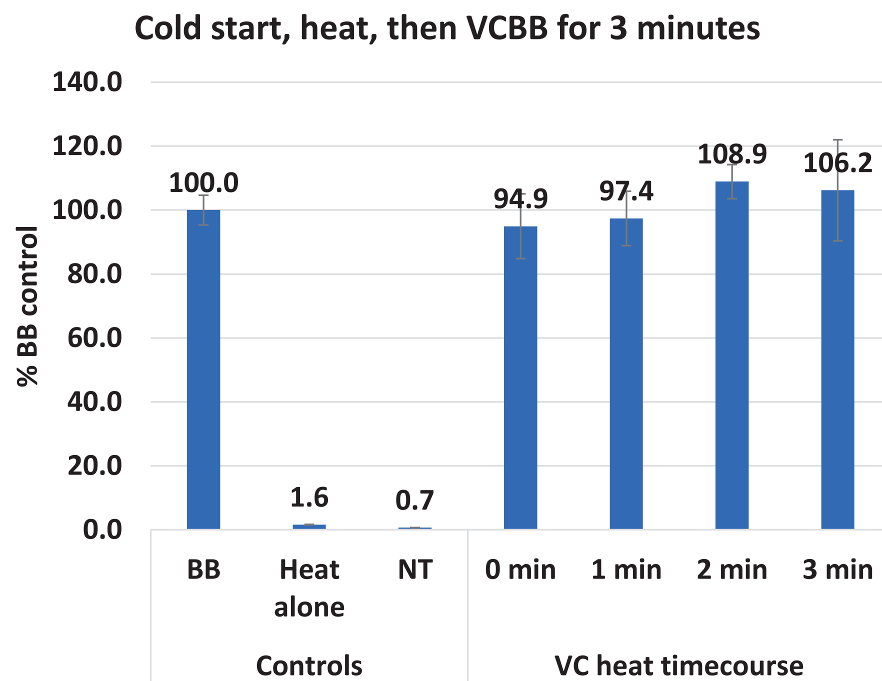
- Lysis efficiency does not degrade at temps lower than 95C – upper right fig.
  - Sample holder *should* (shall?) be insulative enough to maintain temp of at least 65C during shaking
- Nuclease inactivation suffers at temps less than 95C (lower right fig), so sticking with current program of holding 95C for 2 minutes
  - Have not explored lower temp for longer duration – energetically didn't see an advantage. Also easier to keep temp up during shaking by heating higher/shorter.
- Biosafety confirmed for current program (showed images before)



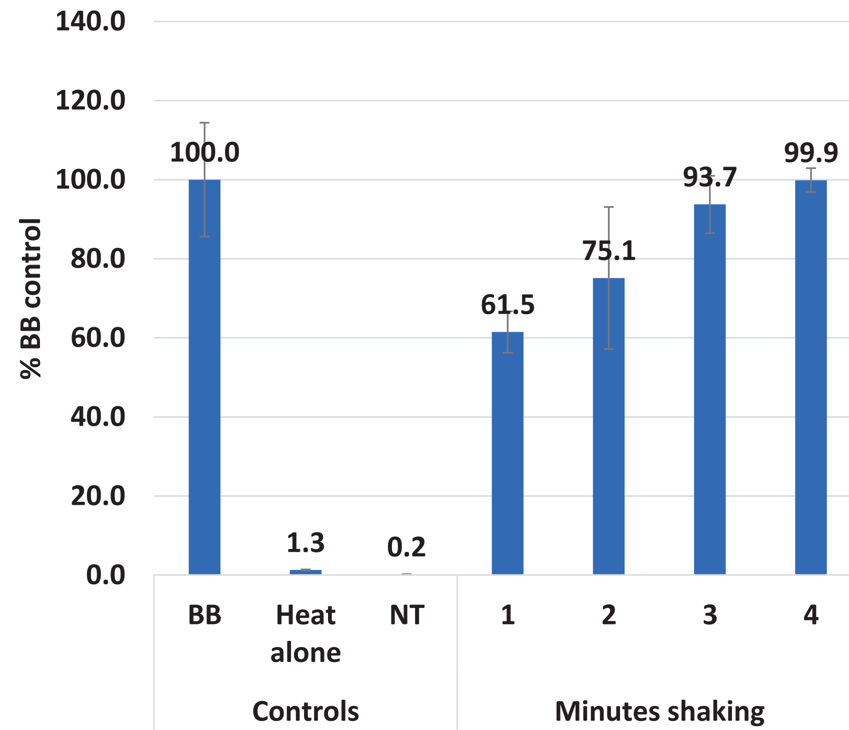
# Durations and timing of heat

- Initial heating ramp is balance between power and time
  - Derived requirement from available time, battery considerations, etc.
  - Currently requires 1 to 2 minutes to reach 95C depending on starting and ambient conditions
- Duration of holding at 95C (2 minutes) driven by nuclease and biosafety considerations rather than lysis efficiency
  - Plot on right shows no to minimal lysis efficiency gains for longer heating times prior to initiating bead beating



# Durations and timing of shaking (bead beating)

- As shown previously (slide 11), no lysis efficiency boost by keeping heater on while shaking vs. switching off heater
  - Assuming holder at least as insulating as current design
  - Slide 21 showed lysis efficiency equivalency for temps down to 65C
  - VCBB ends the 4 minute shake in the 60-70C range, so stays within optimal lysis zone
- Longer shaking provides improved efficiency with decreasing gains
- **In prototypes, want to make timings adjustable to optimize for downstream NAATOS assay modifications**



# Power and battery considerations

- Key requirement is the battery needs to run for 24 tubes w/out a charge, and be rechargeable worst case overnight
- Current heating demands
  - Peak ~35 W during max 2 min ramp from a cold start
  - Steady state heating ~7W for 2 min hold
  - Shaking ~9W max for 4 mins
  - Total 2 Wh per run
    - If efficiently do 6 runs of 4 tubes each, total of 12 Wh per day (1-2 18650 cells)
    - Very unlikely worst-case scenario of 1 tube at a time → 48 Wh per day (5 18650 cells)
      - Probably ruled out by other battery requirements – will need to determine what a realistic worst-case scenario looks like
- Other battery considerations roll into related requirements on total cost, shipping cost and restrictions, etc.

# Will select a single sample tube for compatibility

- Most work to date used a single 2mL tube that is not “squeezy” and does not have a dropper top
- NAATOS requires a squeezy tube with a secondary dropper top
- Determined polypropylene is the best material, now testing various options (examples on next slide)
- Will determine final tube in next ~month, but very unlikely to have diameters outside the 8-12 mm range or mass outside 1.5 to 3.4 g
- Use 150mg of 100um diameter glass beads in the tube
- Break off swab tip in tube and leave it there for duration of sample prep
- When pick final tube, need to confirm no need for dummy tubes for weight balancing purposes

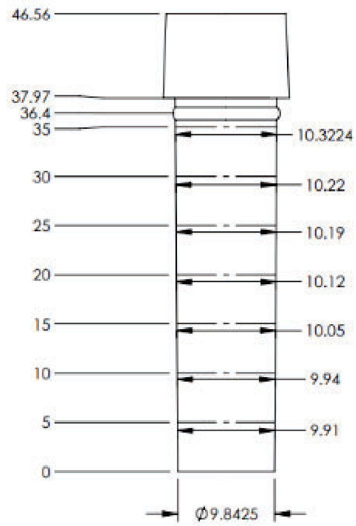
# Sample tube dimensions

1.5 g

3.4 g

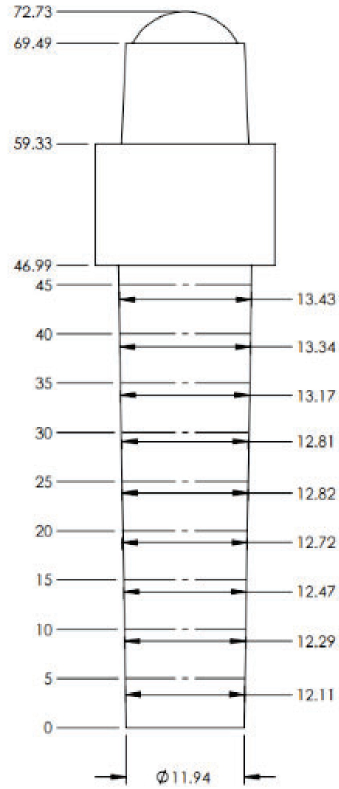
2.3 g

Traditional 2 mL gasketed BB tube



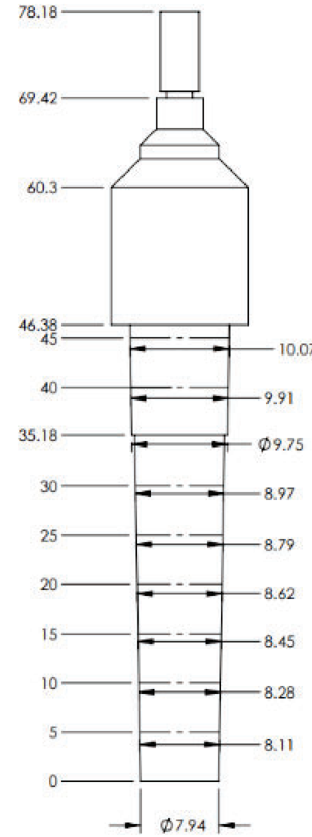

~10 mm

“Wide” tube




~12 mm

“Narrow” tube

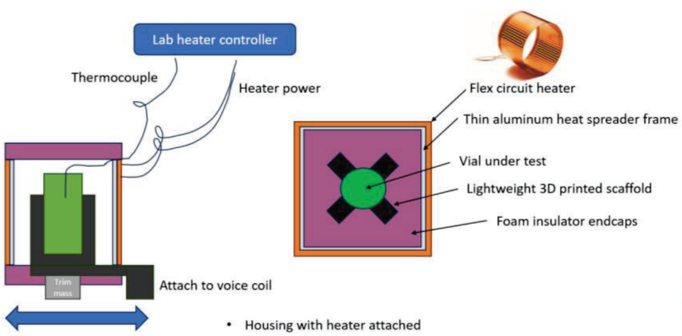


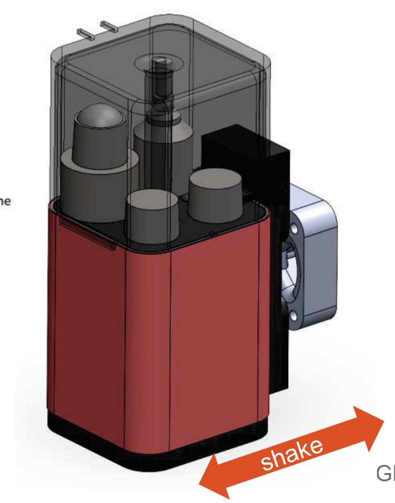

~8 mm

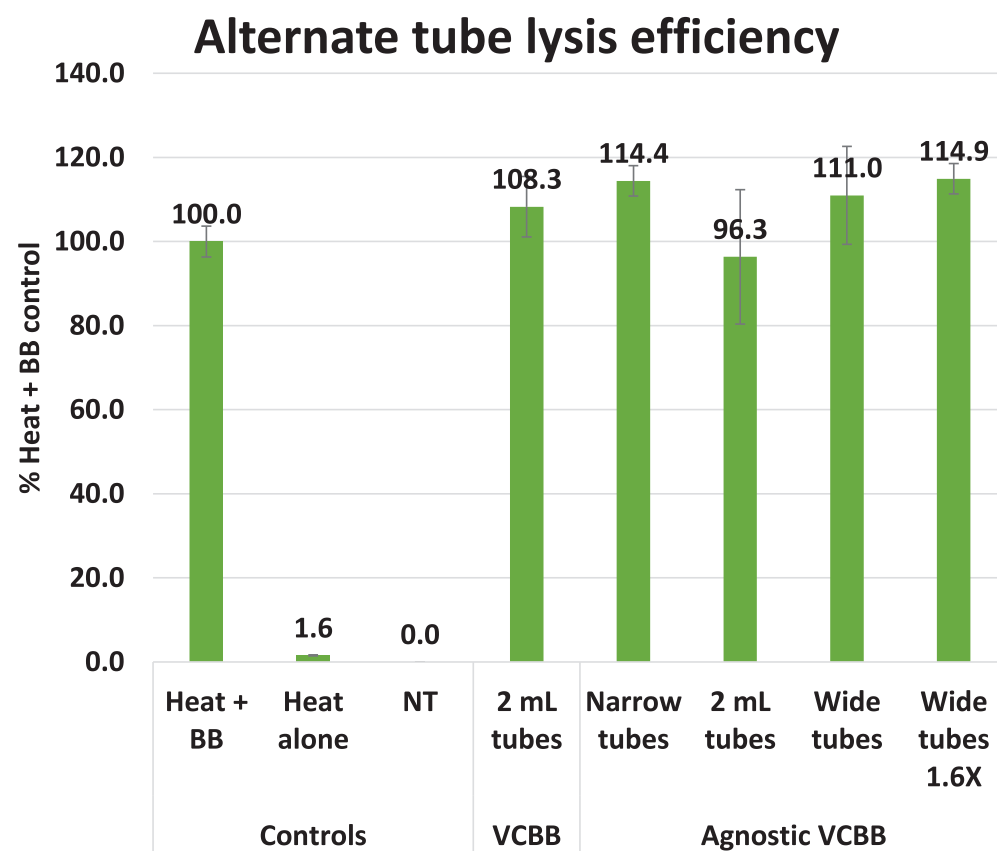
GH+Labs

# Dropper tube performance assessment

- Air coupled heater built to investigate alternative tube sizes in lab
  - Trades time to heat for ease of adaptation for new tube sizes
- Early results seem to indicate that minor variations in tube geometry do not change efficiency substantially



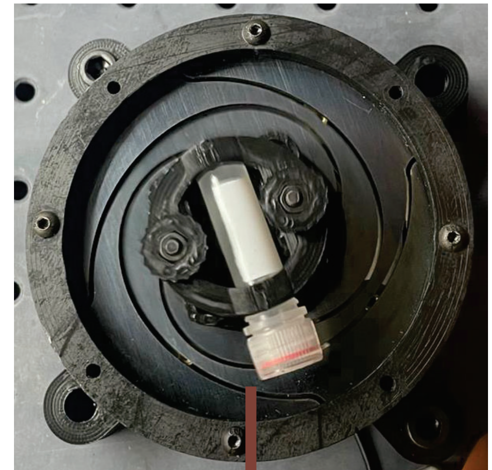
# User interface considerations

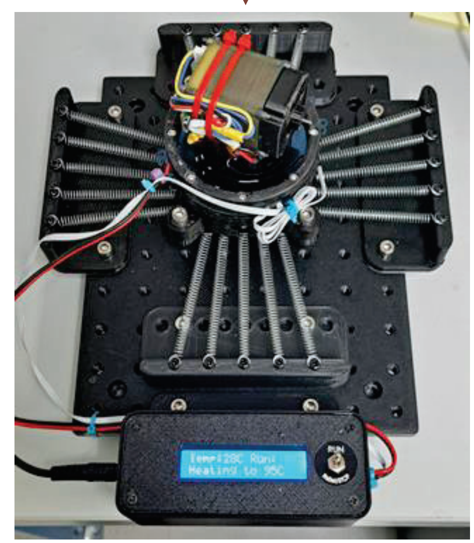
- 1 step, walkaway operation for final unit; prototypes do not have to be
- For final unit, no user-accessible parts or maintenance
- For development – control via updating software or user interface (can be simple computer command line interface, doesn't have to be onboard)
- Indicator(s) of progress TBD
  - Battery/charging status
  - Light colors / blinking vs. simple digital display
  - Indicate heating, shaking, done, still hot vs. just in progress and done
- May need additional "lock out" period to let tube cool before user accesses it
  - User safety
  - Ensuring hot liquid doesn't damage NAATOS device/enzymes

# Current design details

# Voice Coil (History: what is it now)

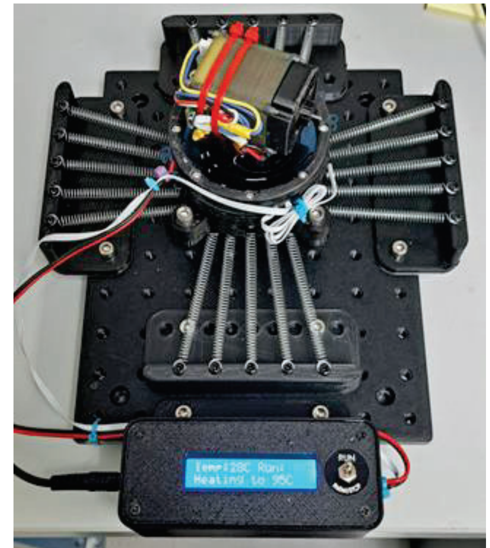
- Path finding unit to explore 3-10mm displacement at 50-80Hz frequencies
- As noted above, initially found efficacy at ~8mm displacement ~70Hz
- Crash task to get lab hardware into the field and add simultaneous heating
- Uganda unit (Rev1) had time pressure to get into the study
  - Unit performed well in the study before encountering a failure (detailed on subsequent slide)

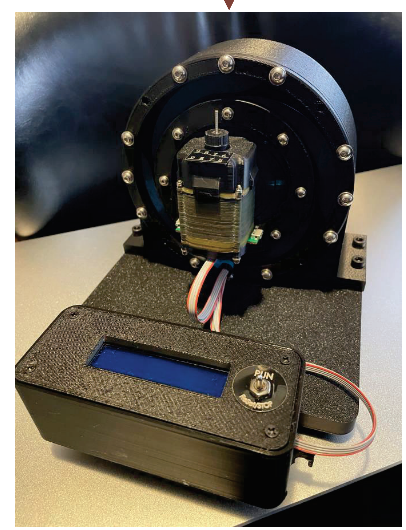




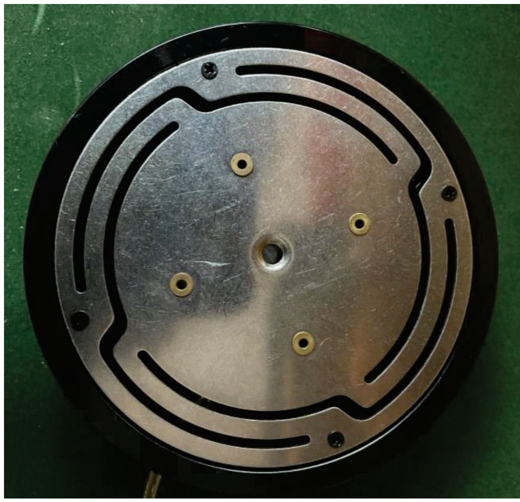
# Voice Coil (History: what is it now)

- During Uganda testing, development continued
- Significant improvements to both the heater and voice coil
  - Three plate flexure and support
  - Improve heater block
  - General clean up
  - Switch to vertical tubes
- Found significant lysis efficiency improvement (>20%) with vertical orientation
- Used some of the improvement to lower frequency and displacement (margin improvement)
- Currently at 7mm @ 64Hz
- Many existing design elements are driven by flexibility prototype-ability and fast turn

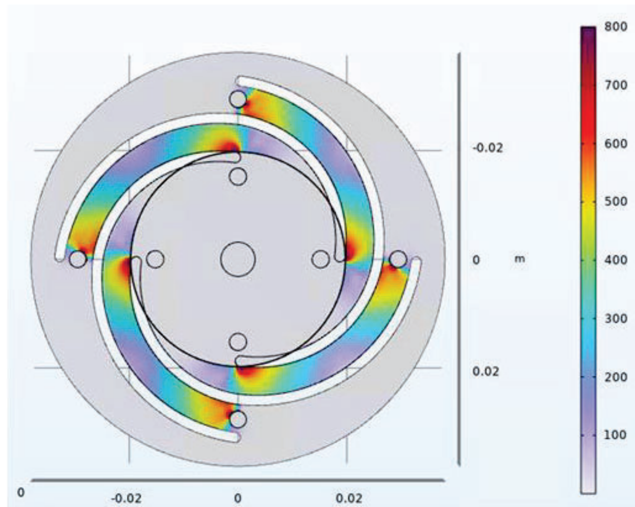




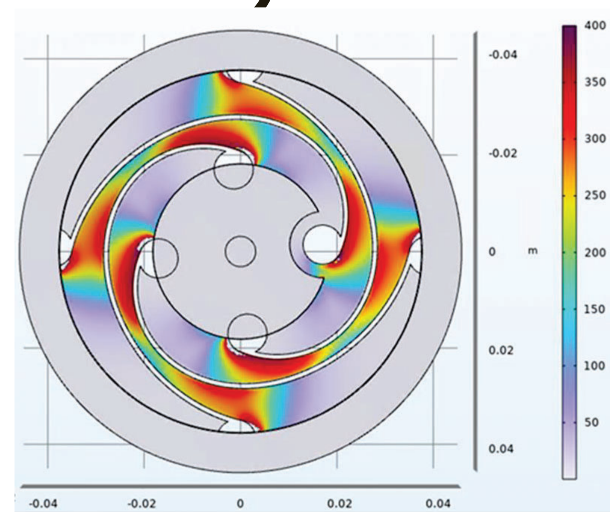
# Voice Coil (Flexure plate geometry optimization)



Off the shelf: insufficient




linear spiral: max 800 Mpa




Tuned spiral: max 400 Mpa

- Distribute the stress on the flexure arms
- Improve displacement to 8mm
- Decreased peak stress by ~3x using geometry alone

# Voice Coil (material selection)

- How much stress relief do we need
  - For extremely long lifetimes we need to be under 600 MPa peak
- Going to stick with 1095 for the time being
  - Some SS are marginally better but with much less availability
  - Titanium is interestingly better, but I don't want to make that jump yet
  - Keeping material as reserve margin

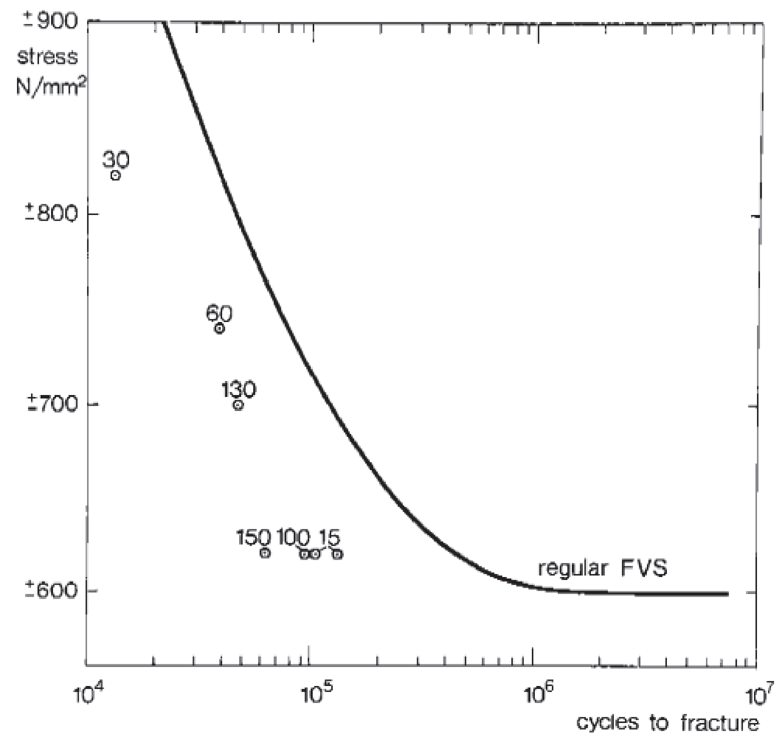



Figure 4
AISI 1095. The effect of pits on the fatigue life. The numbers refer to the pit cross section area in $\mu m^2$.

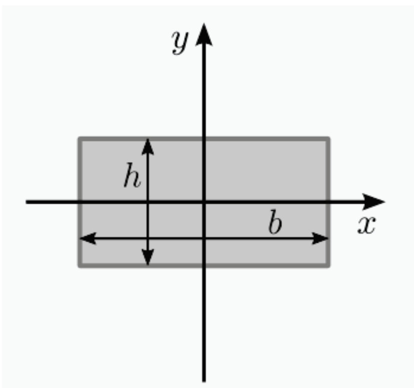
# Voice Coil (material selection)

| Material | Elastic Modulus (GPa) | Yield Strength (MPa) | Ultimate Strength (MPa) | Reversed Bending Fatigue Limit(MPa) |
|---|---|---|---|---|
| 7C27Mo2 | 210 | 1300 | 1800 | 710 |
| Cronidur 30 | 210 | 1850 | 2150 | 1141 |
| XD15NW | 198 | 1580 | 2350 | 1095 |
| 100Cr6 | 207 | 2033 | 2240 | 938 |
| C300 | 189 | 1971 | 2020 | 861 |
| C350 | 199 | 2316 | 2358 | 758 |
| AerMet100 | 194 | 1689 | 1965 | 945 |
| AerMet310 | 192 | 1900 | 2170 | 1030 |
| AerMet340 | 192 | 2160 | 2430 | 986 |
| M50 | 189 | 2200 | 2480 | 1010 |

- More conventional grades may be a good option (420, 316L, etc.) some evidence that they could be close to filling requirements, but good data was not readily available and was not a hole we needed to go down to achieve our experimental objectives

# Voice Coil (need more displacement)

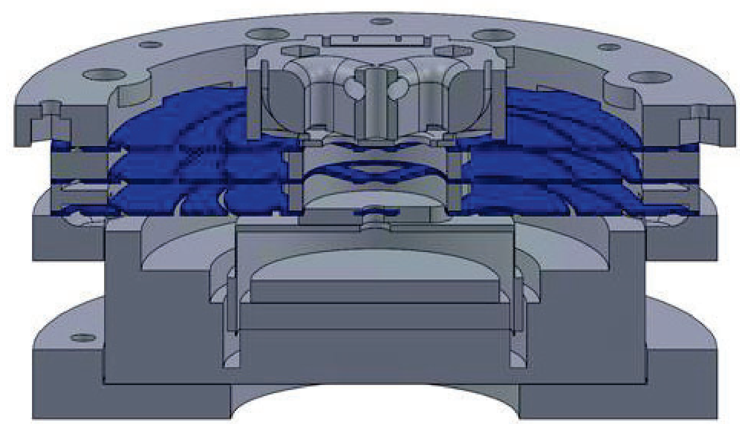
- Final stress optimized design
- Exploit nonlinearity of 2nd moment of area




$$I_x = \frac{bh^3}{12}$$

$$I_y = \frac{b^3 h}{12}$$

- Thinner plates decrease stress in individual plates
- Combining multiples keeps resonance frequency up
- Multiple spaced plates improve the centering of the coil in the yoke
- Three 0.025in 1095 Spring steel plates



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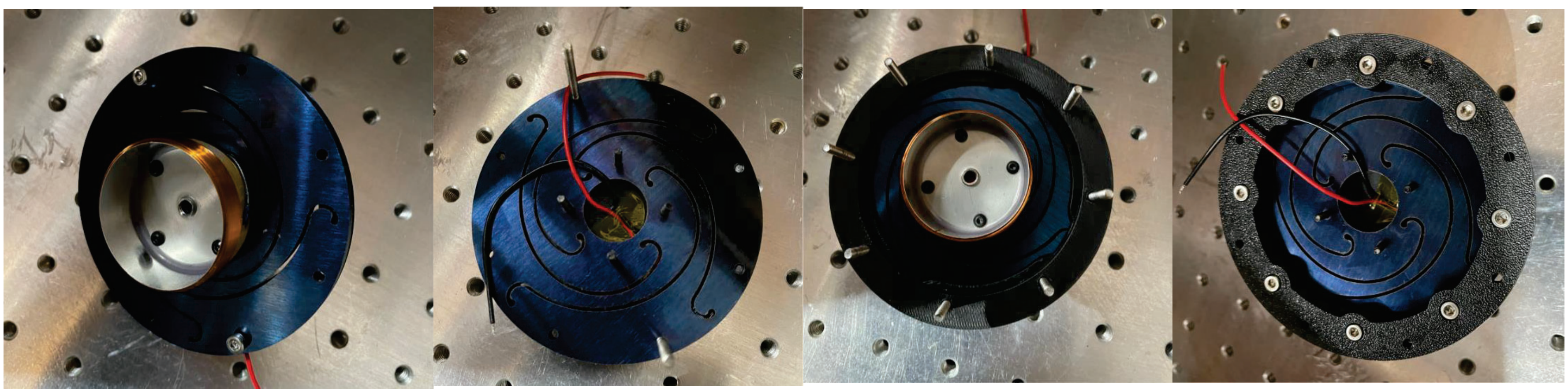
# Voice Coil (COTS parts)

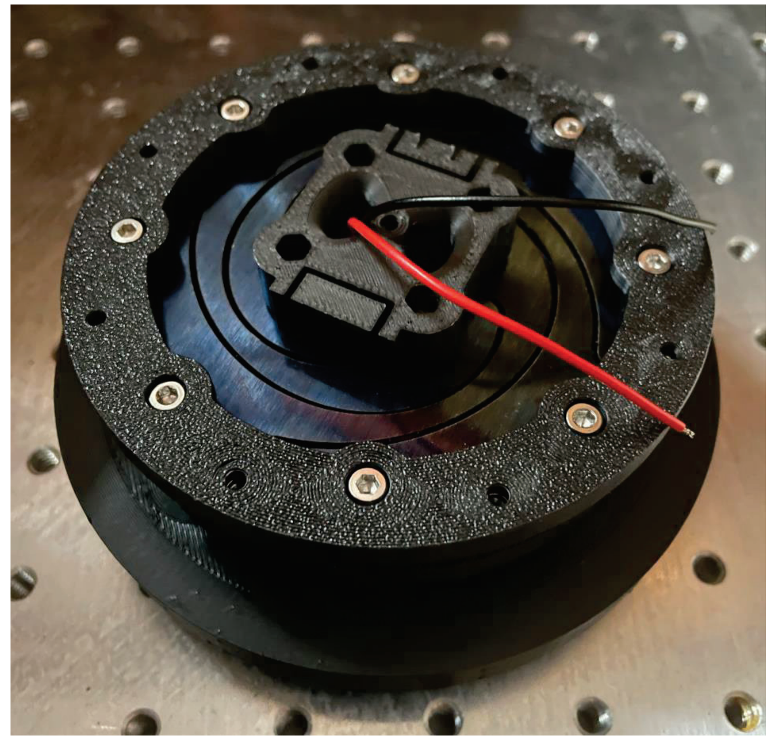
- Leveraged off-the-shelf surface resonator voice coil
- Samtronic, Huasheng (Shenzhen) Technology Limited
  - They will supply just the magnet and coil cup for $22 US
    - Min order: 3k
    - They are interested in making the flexure as well (~2k tooling) this is only preliminary talk, and I am still baselining laser cutting

# Voice Coil (build)



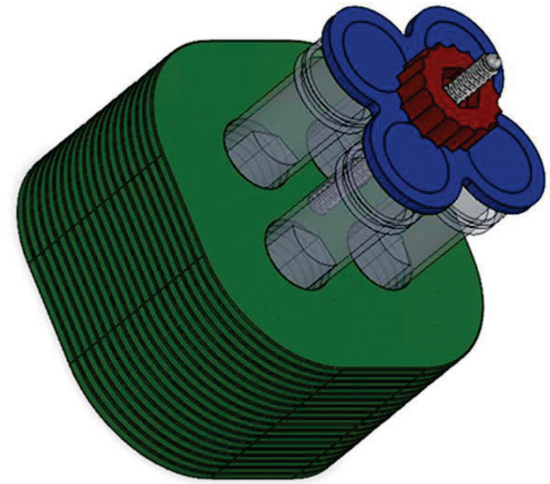
# Voice Coil (build)

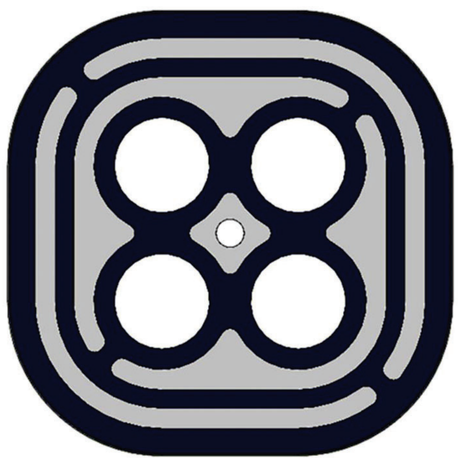
- Off-the-shelf coil
- Three Laser cut flexure plates
- Plastic spacers and screws
- Tested for 4 days of continuous running (22 million cycles)

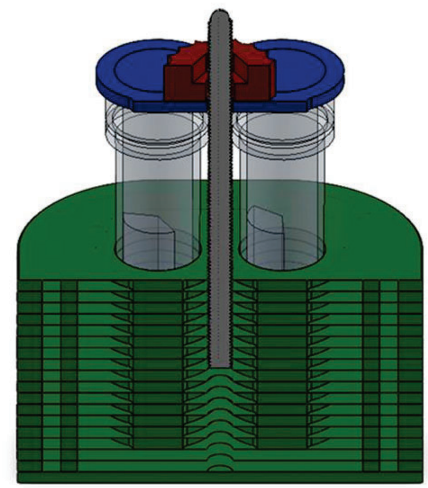


# Heater (original concept)

- Use FR4 for both the heater and the insulation
- Stack on identical PCBs
- Each plate forms a circuitous path for the escaping heat
- Plates stack up like laminations
- Current passes from one plate to the next like batteries

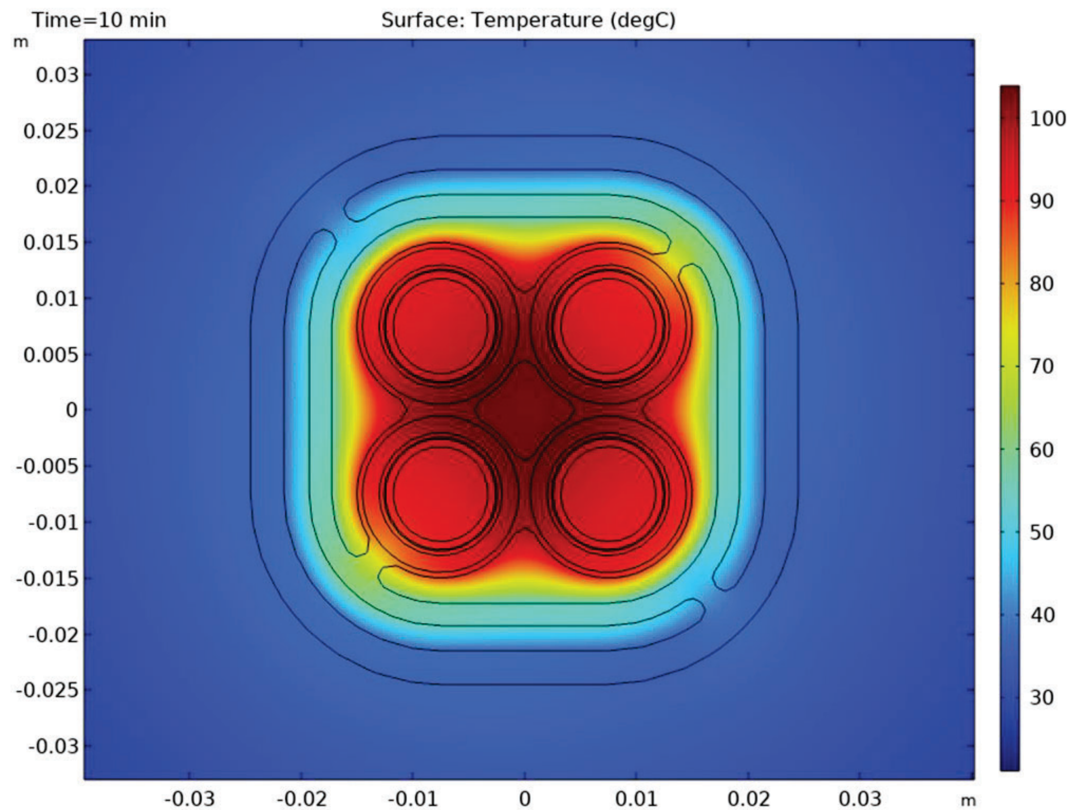






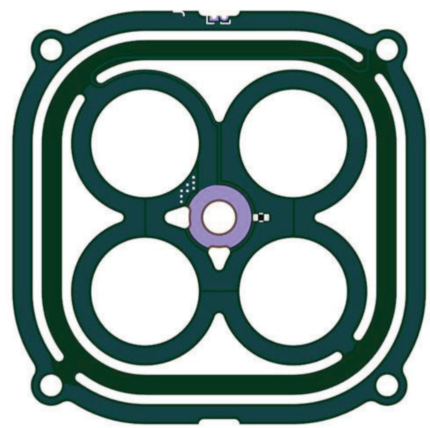
# Heater (original concept)

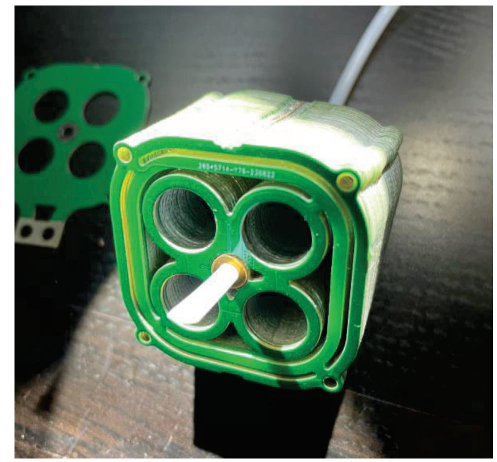
- Using FR4 path provides good thermal insulation
- 45C delta

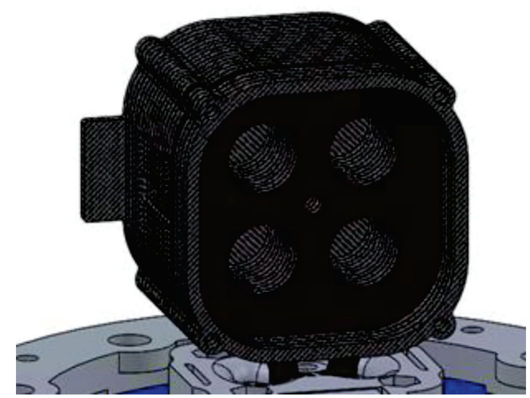


# Heater (reduction to prototype)

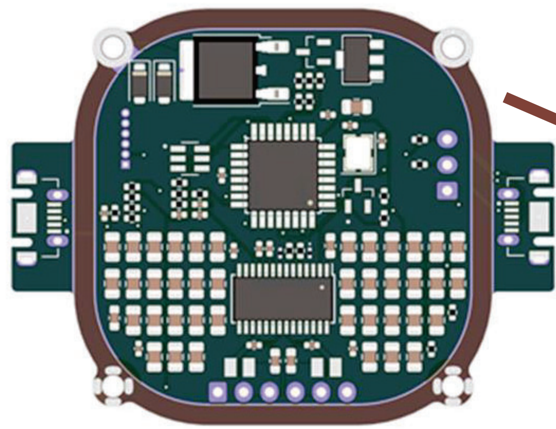
- Simple stack of identical layers
- Forms both a heater and insulation and the body of the unit
- FR4 is cheap
- Currently using 0.8 mm double-sided boards for ease and flexibility
- Wanted to use 4 and 6-layer boards to decrease the number of layers but was becoming a headache

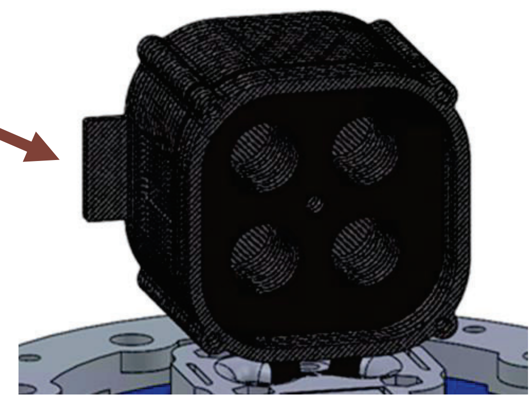






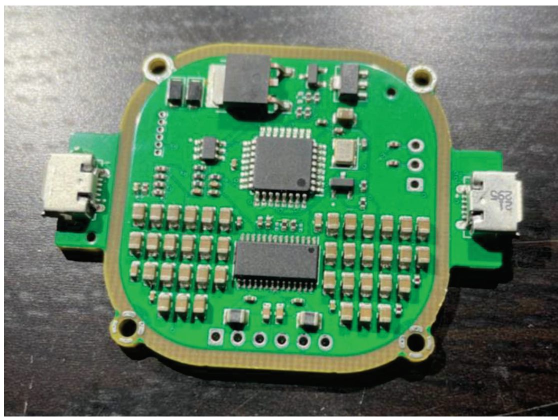
# Control and drivers

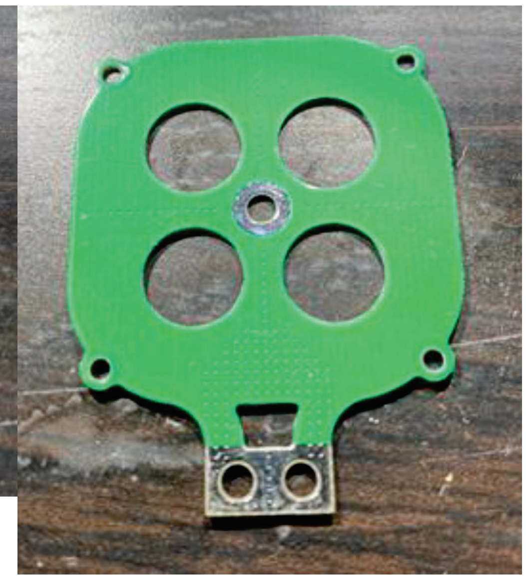




- All on board
  - Microcontroller
  - Class D amplifier
  - PWM PID heater control
  - Thermistor feedback
  - Almost no wiring
- The next version could have no wiring
- Talk about ferrite vs inductor filter
- Heater insulation and control all weigh **80g**

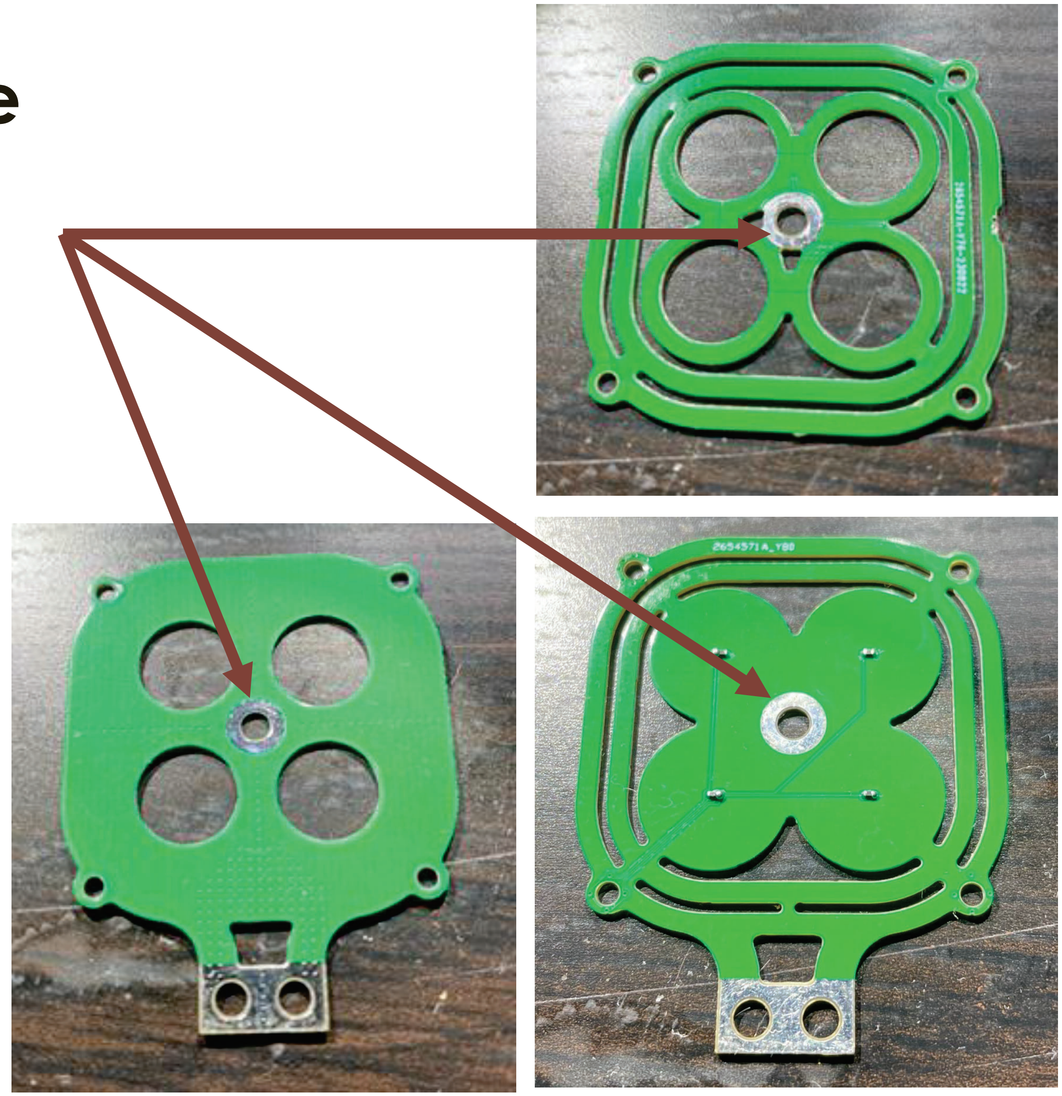
# Components



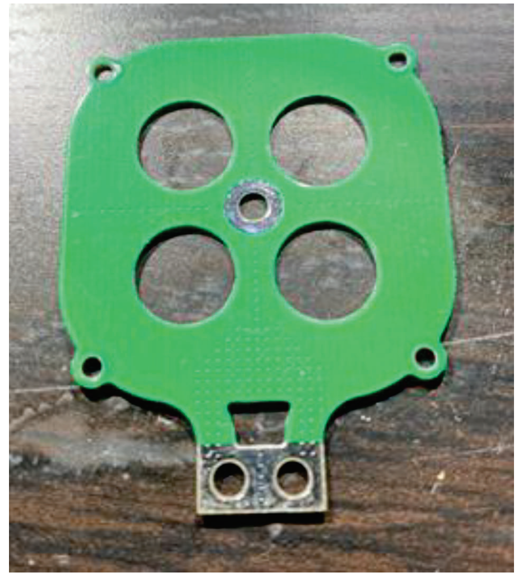
# Reflow assembly technique

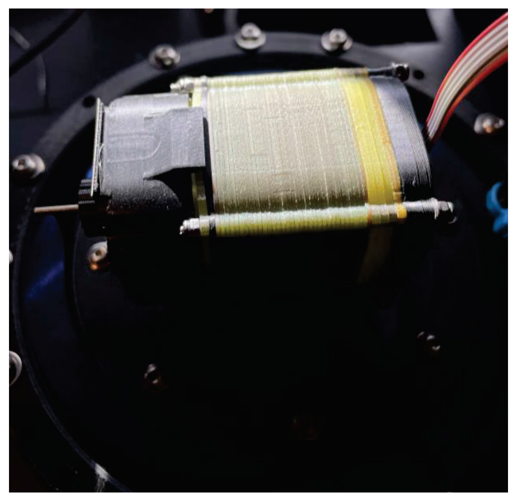
- Low temp solder paste melt temp 138C
- Stack the layers in a jig for alignment and clamping
- Drive current through the heater layers to melt the solder
- Let cool and you have an assembled heater
- Using the heater to assemble itself… priceless



# Monolithic heater assembly

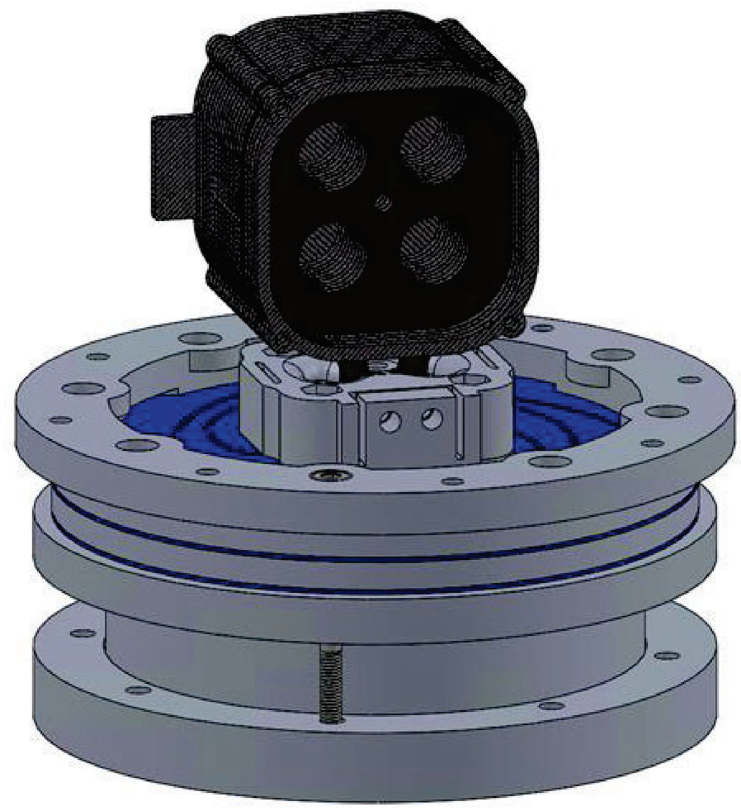
- Option one
  - Glue laminated structure
  - Use thermal cure epoxy during the coil clamping and soldering process
- Option 2
  - The PCB surfaces are tightly held together in the current design
  - Conformal coating could be applied to all laminated surfaces





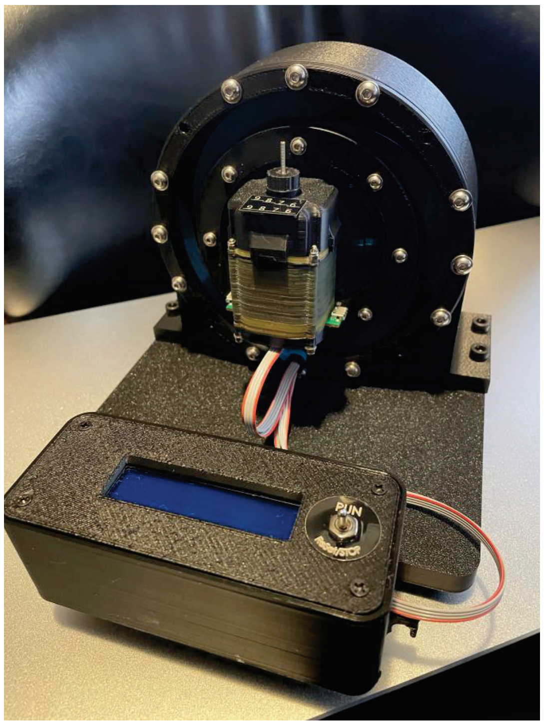
# Bringing it all together

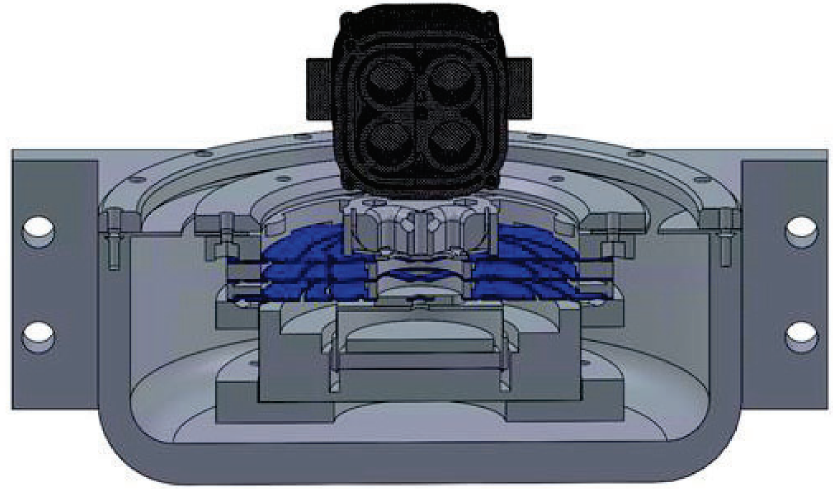
- Current voice and heater situation

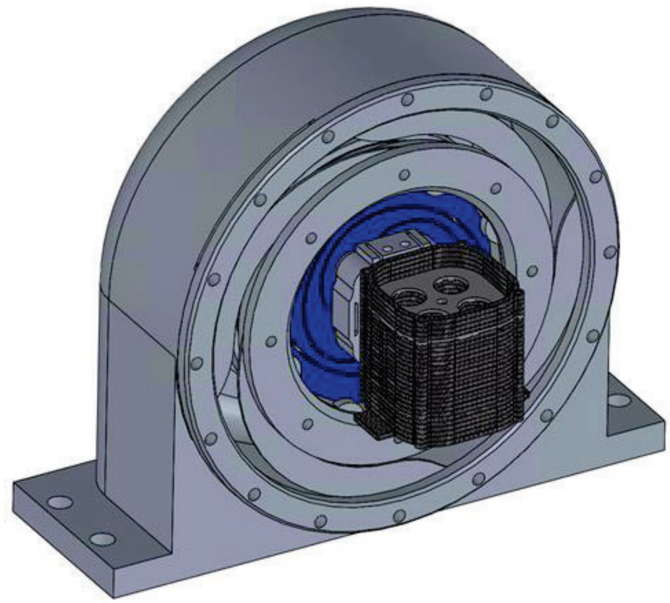


# Bringing it all together

- Coupled oscillator suspension
- Vertical structure

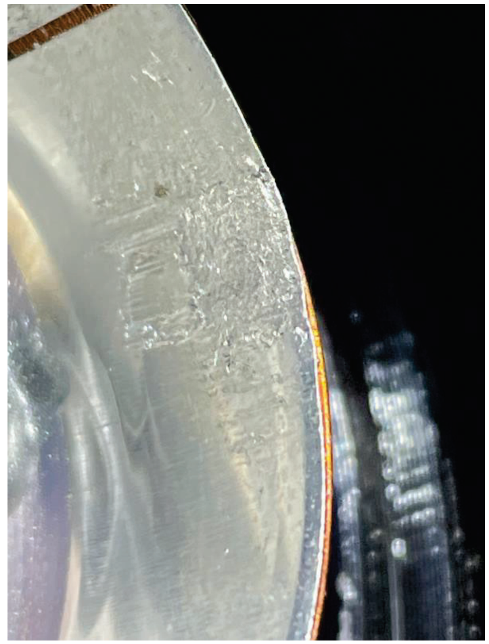






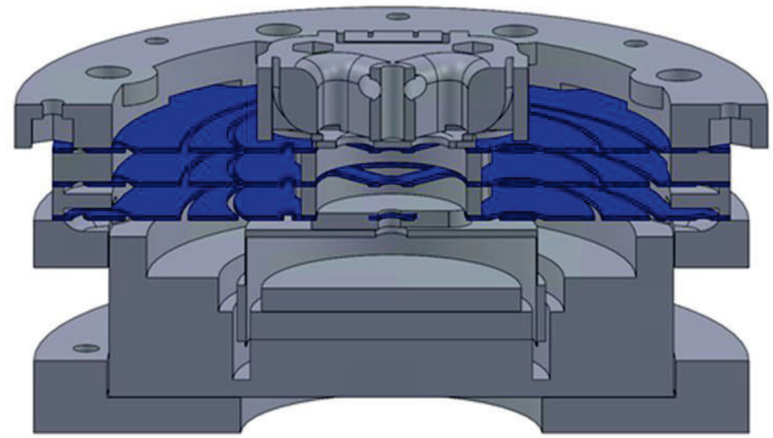
# Failure analysis of Uganda unit (Rev1)

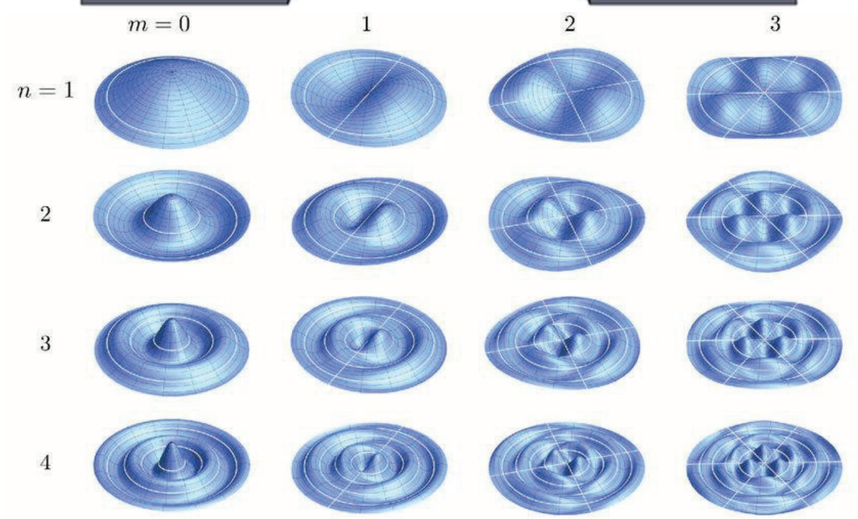
- Observable rubbing of the coil on the yoke
- Unit worked properly after reassembly
- Explains observed behavior
- Flexure plates were intact



# Failure analysis of Uganda unit (Rev1)

- Uganda-era units were a bit flexible transverse to the axis of vibration
- Allowed some m=1, n=1 drum mode
- This was improved before the failure was observed
- Multilayer flexure and better plate support significantly improve transverse rigidity





# Ran out of time/future considerations

- Might be worth doing a custom design on the voice coil
- Boards need conformal coatings
- Time to move to stainless for flexure
- Reflow solder the heater plates together
- Currently using 0.8 mm two-layer boards move to 4 or 6 layers.
- Stack needs conformal coating and/or lamination.
- Route all connections from board to board
- Accelerometer on board to enable closed-loop operation
- ~2000/year is not a lot
- Design is still optimized for flexibility and rapid prototyping
  - Think the basic VC structure is solid
  - The heater may or may not be ideal for this target volume.
    - Maybe more COTS parts
    - Polyimide flex heaters
- Can have zero moving wires by having the UI on the device and supplying 12v on the innermost plate and ground on the outer.

# Initial BOM analysis

| Key parts | Min quantity | Price | Confidence | Note |
|---|---|---|---|---|
| VCA (cup and magnet) | 3000 | $22 | solid | |
| PCB stack for heater and rack | 40 | $0.6 | solid | |
| Copper shim | 100 | $0.4 | solid | |
| Tube clamp | 1000 | $0.5 | ROM | |
| Rack to VAC mount | 1000 | $2 | ROM | |
| Stand offs | 100 | $0.2 | solid | |
| Nuts and bolts | 100 | $0.5 | ROM | |
| Class D amplifier 18W (TPA3138) | 1000 | $0.4 | solid | |
| SamD21 (ATSAMD2118A) | 1000 | $4 | solid | In normal times: $1 we can do better |
| Other electronics parts and PCB | 1000 | $5 | ROM | |
| Vibration isolation | 1000 | $3 | ROM | |
| All else – Case, SPU, battery | TBD | <$50 | ROM | |
| Total: | | <$100 | ROM | |

# Plan moving forward

- Similar to power module, want to push toward cheapest possible solution first
- Schedule and milestones
- Meeting cadence

# NAATOS sample prep module requirements

# Selected Requirements

| ID | System requirements |
|---|---|
| 240 | Sample prep module will be produced at 2000 units/year quantities. |
| 165 | Sample prep module will comply IEC 61010-1. |
| 226 | Sample prep module will comply with IEC 61010-2-101. |
| 229 | Sample prep module will comply with IEC 61326-1. |
| 230 | Sample prep module will comply with IEC 61326-2-6. |
| 246 | Sample prep module will comply with ISO 18113-1 for labeling that provides necessary information for proper use, handling, and identification. |
| 169 | Sample prep module will comply with transportation regulations related to electronic devices containing batteries. |
| 242 | Sample prep module will comprise assembled raw materials available from more than one global supplier. |
| 205 | Sample prep module will cost $200 EXW at 1000 units/year. |
| 228 | Sample prep module will fit on a table within a space ≤ 30 cm deep, 45 cm wide, and 45 cm high. |
| 180 | Sample prep module will have an MTTF of 12,000 ~~cycles~~ runs. |
| 210 | Sample prep module will include a stand-alone power source. |
| 235 | Sample prep module will indicate or enforce correct orientation for loading sample prep tube. |
| 254 | Sample prep module will minimize the burn risk to a user. |
| 214 | Sample prep module will render a sample biosafe during operation. |
| 231 | Sample prep module will support ≥ 24 tests during a power outage. |
| 255 | Sample prep module will visually communicate progress and completion of sample prep process. |

# Selected Requirements

| ID | System requirements |
| --- | --- |
| 206 | Sample prep tube (with reagents) will cost $0.15 EXW TBR at 10 million units/year. |
| 212 | Sample prep tube must contain stabilized lysis reagents for transport and storage. |
| 186 | Sample prep tube will comply with ISO 18113-1 for labeling that provides necessary information for proper use, handling, and identification. |
| 245 | Sample prep tube will comprise assembled raw materials available from more than one global supplier. |
| 190 | Sample prep tube will contain all reagents preloaded in stable form. |
| 188 | Sample prep tube will function as intended within 60 minutes after being unpackaged. |
| 189 | Sample prep tube will have a minimum shelf life of 18 years. |
| 191 | Sample prep tube will not require precise measurements to dispense correct lysate amount into test device. |
| 219 | Sample prep tube will provide printed space for operator to write pertinent clinical notes (e.g., patient ID). |
| 237 | Sample prep tube will remain closed during lysis in sample prep module. |
| 192 | Sample prep tube will require addition of ≤ 1 external reagent prior to insertion into Sample Prep module. |
| 166 | System prep module will require one interaction period to lyse sample. |
| 173 | System will maintain function at temperatures between 5–45˚C. |
| 171 | System will meet ASTM D7386-16-“Standard Practice For Performance Testing Of Packages For Single Parcel Delivery Systems” transport standards. |
| 172 | ~~System will produce a result within 60 minutes~~. Sample prep procedure will take < 15 minutes total including sample collection |
| 176 | System will provide printed IFU (pictorial with English instruction) and on-device labeling (FprEN ISO 18113-1, FprEN ISO 18113-2) |
| 174 | System will use ISO/IEC spec for symbols (FprEN ISO 18113-1, FprEN ISO 18113-2). |
| 177 | ~~System will weigh < 1 kg.~~ More like hand-portable and stable on benchtop while running or sliding the module on benchtop |
| 227 | Tongue swab will remain in sample prep tube after sample collection. |

# Additional not-yet-official requirements / specs

| ID | Specification |
|---|---|
| TBD | The sample prep module will accommodate up to 4 sample tubes at a time |
| TBD | The sample prep module will be operable while charging the battery |
| TBD | The sample prep module battery will be fully rechargeable overnight |
| TBD | The sample prep module will produce lysis efficiency at least as high as the reference assay of heat block + BioSpec bead beater (TBR for NAATOS assay) |
| TBD | The sample prep module will inactivate nuclease activity … TBD |
| TBD | The sample prep module will hold sample tubes in an upright orientation (angle tolerance TBD) |
| TBD | The sample prep module will provide a peak to peak displacement of the sample tube of 7 +/- 0.5 mm in the horizontal direction |
| TBD | The sample prep module will oscillate the sample tube at a frequency of 65 +/- TBD Hz |
| TBD | The sample prep module will heat the sample tube to a maximum of 95 +/- 3 degrees Celsius |
| TBD | The sample prep module should reach 95C within 2 minutes of a cold start |
| TBD | The sample prep module will hold the sample tube at 95C for 2 minutes before bead beating starts. This duration will be adjustable for prototype phase. |
| TBD | The sample prep module will not require simultaneous heating and bead beating to meet performance requirements |
| TBD | The sample prep module will perform bead beating for up to 4 minutes. This duration will be adjustable for prototype phase. |
| TBD | The sample prep module will maintain the sample prep tube's temperature greater than TBD C during the duration of bead beating |
| TBD | The sample prep module will be compatible with a given sample tube, specifically TBD with TBD characteristics |
| TBD | The sample prep module will enable walkaway operation |
| TBD | The sample prep module will not require any user maintenance or allow user modifications to operation (hardware or software) |
| TBD | During the prototype phase, the control software will be updatable via a standard computer connection or on-screen display |

# NAATOS overall requirements

# Selected Requirements

| ID | Product requirements |
|---|---|
| 43 | NAATOS TB V1 must operate within the humidity range of 70% to 90% non-condensing humidity without performance degradation. |
| 44 | NAATOS TB V1 must operate within a temperature range of +5 °C to +45 °C without performance degradation. |
| 47 | NAATOS TB V1 cost per test must not exceed $5 USD. |
| 62 | NAATOS TB V1 must not rely on mains power during test operation. |
| 65 | NAATOS TB V1 must be designed to effectively protect against dust and contaminants, ensuring its functionality and integrity. |
| 68 | NAATOS TB V1 must visually signal that the device is performing as intended to communicate progress and completion of various steps and processes. |
| 69 | NAATOS TB V1 must be a hand transportable product that weighs less than < 1 kg. |
| 71 | NAATOS TB V1 must have a cycle life of 12,000 tests. |
| 78 | NAATOS TB V1 must have a shelf life of ≥24 months for reusable modules and ≥18 months from consumables. |
| 80 | NAATOS TB V1 must support the required daily throughput in the event of power outages. |
| 85 | NAATOS TB V1 must minimize the potential for a burn risk. |
| 86 | NAATOS TB V1 must be registered for in vitro diagnostic use through WHO Prequalification or other regulatory authority of equal or greater stringency. |
| 95 | NAATOS TB V1 must be able to run TBD tests in parallel to support a daily throughput of 10-25 tests per 6-hour day at L0, L1, or L2 health setting. |
| 98 | NAATOS TB V1 must operate without the need for maintenance during its intended lifespan. |
| 99 | NAATOS TB V1 must operate without the need for calibration during its intended lifespan. |
| 63 | NAATOS TB V1 must fit on a table within a space ≤ 60 cm deep, 90 cm wide, and 45 cm high. |
| 50 | NAATOS TB V1 must not require disposal of infectious waste. |

# Selected Requirements

| ID | Product requirements |
|---|---|
| 38 | NAATOS TB V1 must require minimal user interaction periods (<= 3) before walking away and returning to record the result (excluding sample prep). |
| 46 | NAATOS TB V1 must be able to perform more than one sample at the same time. |
| 67 | NAATOS TB V1 must include designated space to accurately record and display patient identifiers. |
| 94 | NAATOS TB V1 must tolerate ±33% variability of lysed sample volume introduced by user into test device. |
| 61 | NAATOS TB V1 must be ready to use without the need for additional components or accessories. |
| 68 | NAATOS TB V1 must visually communicate progress and completion of system processes. |
| 81 | NAATOS TB V1 must not require precise measuring of volume or time required for any step and should instead require number of drops or visual markers. |
| 83 | NAATOS TB V1 must support testing with a noninvasive tongue swab. |
| 102 | NAATOS TB V1 must use no more than two external reagents for sample preparation. |
| 99 | NAATOS TB V1 must operate without the need for calibration during its intended lifespan. |
| 98 | NAATOS TB V1 must operate without the need for maintenance during its intended lifespan. |
| 66 | NAATOS TB V1 must prevent the escape of amplifiable material into the testing area. |
| 75 | NAATOS TB V1 must achieve a clinical specificity ≥ 98%. |
| 74 | NAATOS TB V1 must achieve a clinical sensitivity ≥ 80%. |
| 53 | NAATOS TB V1 invalid rate must not exceed 2%. |
| 63 | NAATOS TB V1 must withstand resistance to shocks and vibrations from drops by users of 90 cm TBR height without performance failures. |
| 248 | NAATOS TB V1 must indicate to users that the test is invalid. |
| 85 | NAATOS TB V1 must minimize the burn risk to a user. |

GH+ Labs

# Thank you