Immediate joint infection diagnosis using bed-side iPhone live imaging

AUTHORS AND THEIR BACKGROUND:

1) **Lead author Sebastien Stephens (MD PhD)** is a Harvard-trained live imaging specialist with a proven research track-record and strong orthopaedic, trauma and rural training in QLD.
2) **Prof Keith Grimwood and Dr Kay Jones** (infectious disease specialist/microbiologist) at Gold Coast University Hospital will benchmark the project to current hospital standards.
3) **Alexandre Stephens (PhD)** is the Director of Research of Northern district NSW and a biostatistician who will ensure appropriate study design and analyses.
4) **Dr David Bade** is the director of Orthopaedics, Queensland Children's Hospital
5) **Dr Adam Coltzau** is the Clinical lead, RDAA and ACRRM Rural and Remote Response

INTRODUCTION & AIMS

Joint infections are morbid, costly and most importantly, difficult to diagnose especially in the rural/remote general practice setting. We propose a system of simple optical beads attached to an iPhone to immediately identify live bacteria with a single drop of joint aspirate.

HYPOTHESIS

The iPhone-optical bead system through live-stains will identify live bacteria promptly and of clinically-relevant significance; decision to proceed to theatre/emergency decompression/transfer.

MEASURABLE OUTCOMES

1) Time to treat (locally/transfer)
2) Morbidity
3) Mortality

STUDY DESIGN

A cohort prospective pilot

METHODS

To establish sensitivity & specificity & positive/negative predictive values against standard hospital lab procedures (gram stain, cell count and culture), non-harmful bacteria will be used in a university lab. The trial will subsequently use (1) control normal synovial fluid +/- live stains (LIVE BacLight) and (2) known infected synovial fluid to test and benchmark against gold-standard hospital microbiology laboratory protocol. Power calculations (α 0.05, β 0.2) estimate a sample size of 125 (paired controls – comparing lab-based gold-standard to our method) to estimate a sensitivity of 0.97 with a 95% CI of 0.94-1.00, based off Hajian-Tilaki (2014). We have sought Human Research Ethics Committee approval.

The basis of our methodologies are simple as exemplified below.

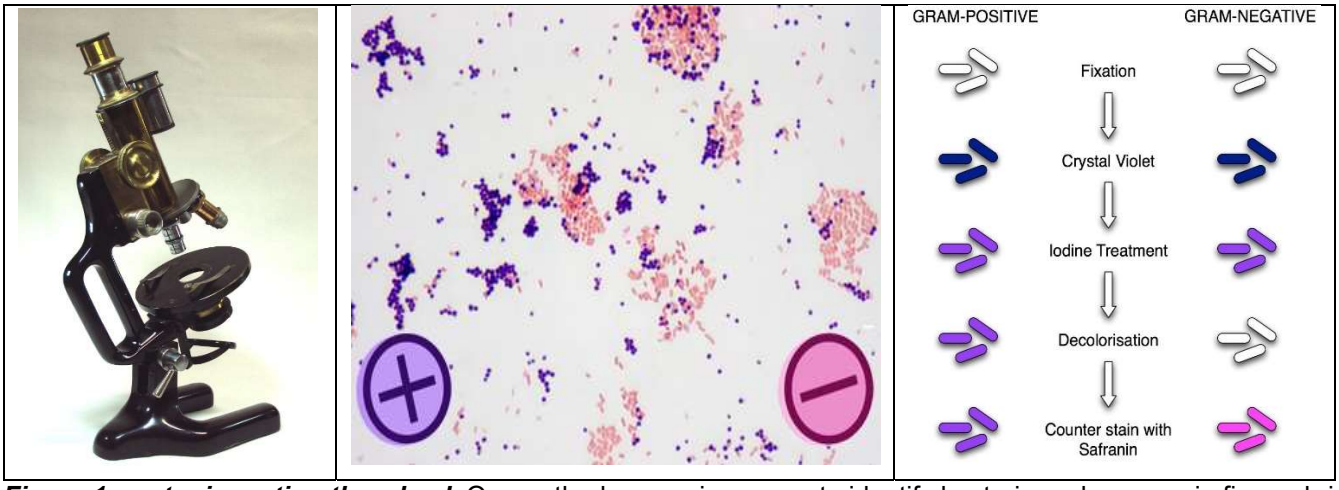

Figure 1 - not reinventing the wheel. Our method uses microscopy to identify bacteria and as seen in figure, bring this to the next level by using fluorescence, much like fluorescein when examining the cornea for uptake/damage.

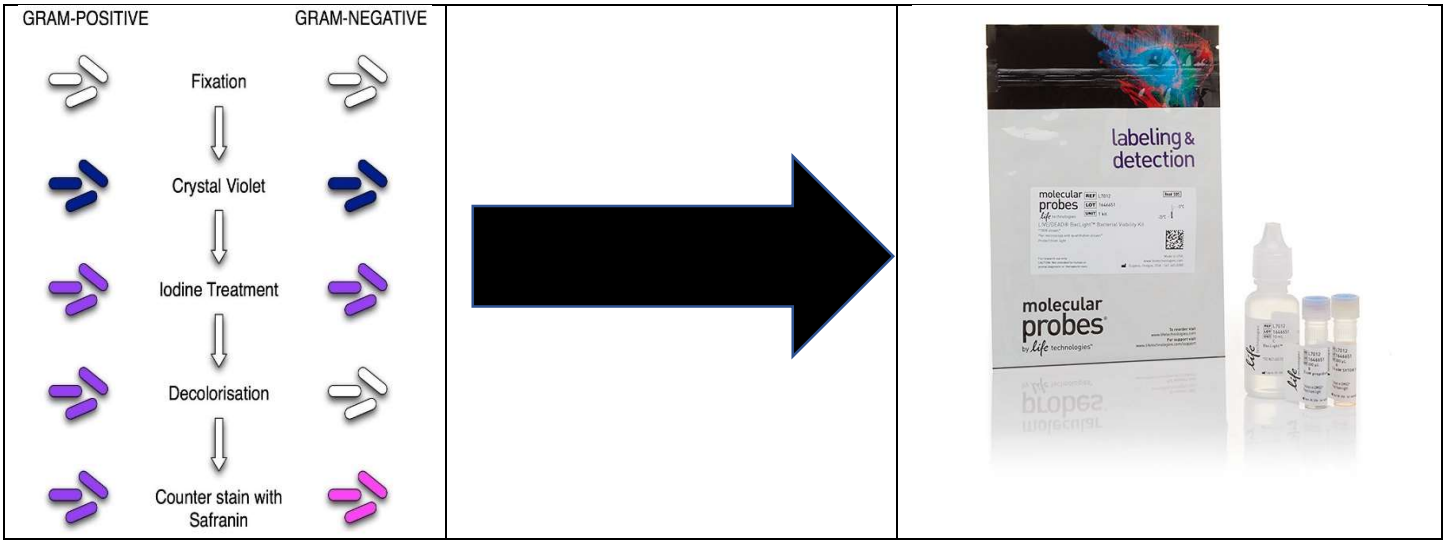

Figure 2 – bring it to the bedside safely. *By using a fluorescent gram-stain, we can use regular GP practice fundoscopy tools or slit lamps to create fluorescent light to identify bacteria.*

Figure 3 – real example of our technique. Joint aspirate is performed followed by addition of bacterial-specific dyes and then viewed under a portable microscope (insignificant cost) with a real example image on the right.

ANTICIPATED COSTS

LIVE BacLight™ Bacterial Gram Stain Kit		$1,100.00
Research Assistant/GP registrar (6 months FTE $41.96/h)		$41,456.48
Microscopy (OlympusLaser Confocal Microscope) (10 hours x $30.00)		$300.00
Invitrogen phosphate buffered saline	Catalog number: 70011069	$70.00
Nunc™ Edge 2.0 96-Well Plates	Catalog number: 167542	$359.00
Select Agar™, powder	Catalog number: 30391023	$291.00
Biostatistician	(2 hours x $125)	$250.00
Ethics advisor/writer	(6 hours x $40)	$240.00
Total		**$44,066.48**

PRILIMINARY RESULTS

10 patients present to a MM6 hospital with symptoms consistent with septic arthritis. With the methods employed above, and the simple blue light from a portable GP fundoscope, live-video imaging was produced from joint aspirates. We were only able to identify white blood cells (for which cells counts were created using a simple haemocytometer (standard handheld lab method) and using light refraction, the **findings for all patients** were not consistent with organisms. These were subsequently proven by X-Ray (chrondrocalcinosis) and lab MCS as analysed (gold standard) by QLD Health Pathology. These patients were successfully treated for gout and **resulted in a savings of $210,000 in flights**.

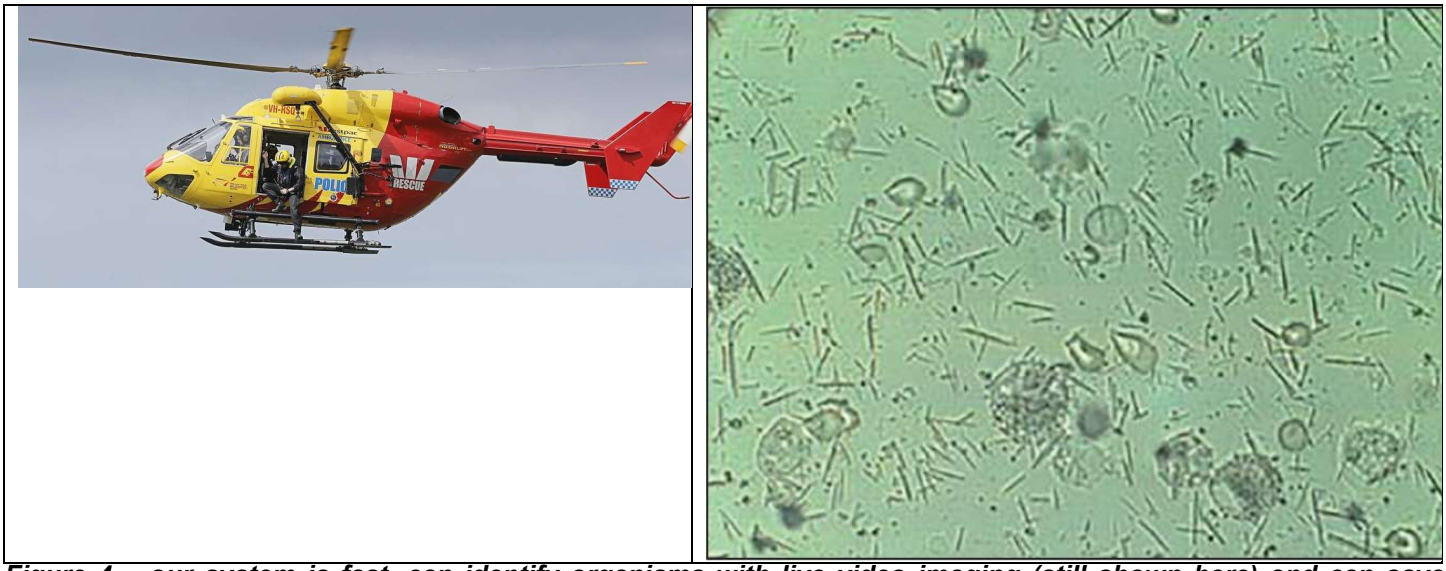

Figure 4 – our system is fast, can identify organisms with live video imaging (still shown here) and can save hundreds of thousands of dollars in rural settings. *The left image shows the Westpac RSQ helicopter used in QLD to fly critical patients to tertiary institutions. The right image shows gout in a patient we live-imaged.*

LIMITATIONS

1) Autofluorescence
2) Until (1) is resolved, true specificity and sensitivity is limited

MOVING FORWARD

1) A new microscope is being developed.
2) At the cost of ~$300, every person with a smart phone in the rural setting will decrease morbidity and costs.

CONCLUSIONS

We developed a cleanable, pocket-size device which permits to see microorganisms immediately. Testing has proven robust with video footage showing live bacteria with the iPhone set to video mode. However, the device has limitations with resolution and autofluorescence. Thus, we are still in the process of establishing sensitivity and specificity of the device in the lab environment. With basic/optical science hurdles ironed out, we will continue to, as planned, into the abovementioned human pilot trial.

The expected benefit is of broad application from septic paediatric native hip arthritis to prosthetic joint infections. Its significance extends to expedite patient care with measurable outcomes (time to diagnosis, time to theatre and cost). Since human joints are sterile, no live bacteria should be found, thus on-the-spot diagnosis is theoretically possible and importantly also that of gout and pseudogout which are major differentials with almost identical presentations. Moreover, since not all bacteria are readily mobile, our methods testing to identify bacteria through use of commercially-available (published) permeable live stains which can identify any cell with a nucleus (ie mycoplasma) to increase video contrast is likely to advance the management of joint infections in the rural setting as well as world-wife urban settings.

REFERENCES

1) Haddad 2017
2) Porrino 2020
3) Fehring 2020