



Breakout: Cancer care

Led by Professor Poulam Patel
and Professor Helen Byrne

Facilitated by Professor Nicky James
Supported by Dr Tanya McCallum



Summary for feedback – Cancer care -1



- To personalise the dose and treatment, there's an unmet need in sensors and measurements “Is the drug hitting the target?”
- Side effects v Efficacy – what's the optimal dose?
- Not fully explored what would be useful to measure
 - hypoxia (low oxygen)
 - Immune parameters (cytokine levels eg IL 10)
 - pH
- Scope for feasibility studies that take existing sensors and measure the above

Summary for feedback – Cancer care -2



- Developing tracers to monitor drug levels /efficacy
- Developing tracers/sensors to monitor emergence of resistance
- Developing bio-reactors to model what's going on in vivo
- Injectable/implantable sensors - convert optical signals to something else eg electrical signals in order to detect reagent in real time
- Smart release treatments (based on what is monitored)

Summary for feedback – Cancer care -3



- Linking remote patient diary data / wireless continuous monitoring with side effects and efficacy
- Exploiting - non-invasive measurements eg breath, urine, sputum Can detect eg VOCs
- Involvement of patients in development of new therapies/approaches



Breakouts : Intensive care

Led by Professor Andy Norris
and Professor Declan Bates

Facilitated by Judith Underhill
Supported by Dr Jasmine Harvey





Clinical challenges / opportunities

- Ventilation, Multiple medications – and their control
- Adjusting drug dosages
- Non-invasive monitoring – physiology and metabolic monitoring
- Intervention – twice daily? V continuous
- Continuous sensing
- Monitor – ph etc.. Real time
- Data collation, integrating data and understanding patterns, personalised monitoring – in relation to closed loop systems
- Difficult data extraction, simple software patterns
- Big data sets essential for testing algorithms
- Machines not built to store huge amount of data
- Decision-making based on data patterns
- Sensors must be multi-parameter to be compatible and integrated
- Sensing in continuous systems
- Objective measurement of pain? In a closed-loop system

Non-invasive-v-invasive

Scientific challenges /opportunities



- Definition of closed-loops – varies- in different contexts. Standard: Information fed back and used to change status of the patient
- Aim: to make the loop autonomous



Potential Projects

- Objective measurement of pain/sedation/distress - Need solution?
- Multi-parameter drug/metabolite sensors with drug delivery (& elimination)
- Early (pre-ICU) identification of sepsis
- “Brain probe” (non-invasive!)
- Data – collection/analyses – algorithm/machine learning/pattern
- recognition
- Genomics – rapid screening



Breakout: Chronic wound care

Led by Professor Lt Col Steve Jeffery
and Professor Steve Morgan

Facilitated by Rob Watling
Supported by Dr Sarah Bolton





Clinical challenges / opportunities

- Site of treatment – hospital v community. Usability by all HCW in all settings.
- Diagnosis when under a dressing – primary signs (heat, swelling, redness etc). Can these also be biomarkers for sensing?
- Other dx methods – Doppler (blood flow), ABPI (difference in blood pressure at brachial v ankle), VOC signatures,
- Change dressing daily? Depends on independence v District nurse
- Use of apps for monitoring
- Early detection (what markers – moisture levels etc?) and infection prevention – specific bacteria? PoC testing – ward or community
- Smart tech to decide if District Nurse to visit – run from ?GP surgery? Could also trigger if further intervention required by clinician.



Clinical challenges / opportunities

- Re-infection – use same signs and symptoms
- Prevention especially in SCI patients. Substitute sensory system e.g. sensors in fabric (pyjamas). Link to e.g. change position of/in bed for bed/pressure sores.
- Cost and how affects adoption – health economic case. Focus on the 10% of patients (elderly, diabetic, co-morbidities) who will have wounds that take long time to heal/never heal? Is this a barrier to exploring new technology.
- Where injury is suffered – civilian v military



Clinical challenges / opportunities

- Tech e.g. fitbit, smart watch, to promote good healing e.g. not smoking, tracking image size
- Negative pressure dressing for surgical wounds – limited data. Dryer wounds promote healing? How can this be adapted for wound treatment? Sensor/colour changing chemical built in to sense bacteria as not changed daily. Colour change related to types of bugs? Analyse fluid or gas (VOC) in suction device?

Scientific challenges /opportunities



- Polymer networks to deliver drug (anti-microbial) could also incorporate sensor (moisture, pressure) to know if drug was needed. Controlled delivery.
- Best biomarker. Would prefer something more specific but do we know what it might be...bacterial metabolites, aerobic v non-aerobic, cytokines, quorum sensing molecules, proteins, VOC. There might be info/markers already out there - QinetiQ (Malvern). VOC machine can also measure humidity. How best to harvest the bandage for assessment – nothing lost.
- Colour changing bandages/dressings irt pH or other marker.
- Surface markers reflecting deeper tissue changes? Bio-electrical impedance measurements? Link to e.g. change position of/in bed for bed sores.
- Material that might incorporate multiple sensors – no change to current care pathways/methods. Synthetic fabrics with coating to promote healing etc.



Scientific challenges /opportunities

- Changes in temperature – increased blood flow in wound, sloughing material is cooler, differences in margins but affected by multiple factors in environment
- Biological dressings that incorporate cellular material to promote cell growth and healing – difficult in community setting or for widespread adoption
- Incorporate anti-microbials into dressings – multiple issues including resistance
- Medical device that can be placed in home to assess the wound – maybe better for older patients
- Imaging – could pick up some colour changes, size changes etc. Not possible in all patients. 3D imaging via image from nurse – track and trigger for escalation? Hyper-spectral cameras? Volume of wound?



Scientific challenges /opportunities

- Modelling – machine learning + clinical notes, mathematical notes. Needs data and relevant sensors to get the data. Existing models on wound healing and tissue regen. What do we want it to do? Often used if cannot measure what we want – might be useful here.
Variation
- Prediction and outcome modelling - often too complex.
- Pressure ulcers – 30% caused by functional medical devices e.g. orthoses, prosthetic, masks. ? Smart actuators to reduce effect?
- Prevention of healing – early damage markers e.g. lactate/pyruvate ratios.
- Best start to treatment – is there – compression, hyperbaric oxygen treatment – difficult to get seal



Gaps

- A clear and measurable biomarker(s) have yet to be identified. Needs to be validated (in vitro and in vivo) and translated to a clinical outcome. What are the thresholds that need to be defined?
- Combinations of biomarkers?

Potential projects

- Biomarkers
 - specific bacterial markers
 - metabolites e.g. lactate/pyruvate
 - VOCs
 - primary signs, pH, moisture
 - combinations of
- Biomarker translation to treatment or clinical outcome
- Open wounds inc negative pressure dressing
- Prevention
- Data gathering and modelling



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Raw notes

- The remains of this presentation are raw notes from the cancer breakout – I have not edited them and they are very rough, so beware!



Clinical challenges / opportunities

- Unmet need in sensors and measurements
- Min exposure/ max efficacy – measure the exposure using a tracer – not too toxic. Target therapeutic index
- Most cancer drugs, dosage based on about 8 people. When you get too many side effects, lower the dose. Not much monitoring involved. All empirical. Do you need diff tracer elements based on the population eg children. Can we base dosage on measured values? Should reduce side effects.
- How much variation per individual tolerating dose? Big.
- Biological agents – optimal dose is different.



Clinical challenges / opportunities

- What do you measure? Renal function
- Blood measurements not so useful for chemo
- Imaging used – depends on imaging modality – size of what it can detect.
- Tracer – treatment tracer, and response tracer.
- You can detect level of activity – how small?
- Think about sensitivity of measurement technique.
- Data is not mined. Can't predict effectively who will get side effects. What are you basing the decision on? Trial data – profile the patient on age and decide.



Clinical challenges / opportunities

- Could you measure circulating DNA to pick up other mutations arising?
- B-RAF cells – phosphorylated detection
- Need to know you're treating the right patients with the effective treatment.
- Patient view – an app for high risk population (healthy) to measure skin. Personalising treatment. Novartis have developed a side effects app – tracks side effects in real time to see how reacting. Some patients want some control. This is subjective. Can this self assessment of how they feel correlate with a measurement? Sensor that senses drug level? Needs to be non-invasive if regular long term.



Clinical challenges

- Higher risk patients could tolerate tests on more regular basis?
- Are there platforms for sharing side effects? Anonymised shared data might be accepted. There's a platform 'Open humans' where patients get to choose which projects use their data. Laziness is the barrier – could uploading be automatic?
- At the moment we don't exploit data we currently have. Not reliable enough to stop or change treatment. Not reliable = knowing that a 30% chance of side effect wouldn't change your decision, whereas 95% might.
- We don't know how patient is handling the drug or what's happening to the tumour.
- Markers can be patient specific. Can't compare to average.
- Resistance can be a big challenge. When should you change/ try different earlier/ have holiday? Can help with modelling. Sensors needed. Involves a refractory period beyond which you can't go back. Don't want to push them to the edge of when they'll develop resistance. Modelling opportunity. Can we get a biomarker or readout to inform.
- Could run parallel model with patient treatment. Look at how the invitro model responds



Clinical question

- How do you decide what to give? Lab tests show what drugs work best on which cancers. Trials. Patient groups based on risk groups.
- You can make a decision but maybe 40% patients won't respond. Don't know why. Genomic data might help. Measure dynamically/quickly if it's working then could switch treatment.
- Chemo – chances of harm:good
- What time window before make decision? Weeks 2-3 weeks. If someone has scan – 2-3 weeks before treatment/ operation. Genomic info if in the 2 weeks can inform. Genomics not yet advanced enough to know if they will have a long response.
- Does location of biopsy make a difference? Yes. Work being done on heterogeneity of tumour.
- Proteionics has been underwhelming so far. Nobody uses it.

Scientific challenges /opportunities



- Longer term - Something embedded monitoring for a long time and only sends off data when a threshold is passed.
- Short term
- Possible to measure any drug in blood. Is there sufficient opp to measure side effects developing? People can develop in diff ways? Can you do test to predict side effects.
- Reporting side effects is standardised. Can you measure continuously that tells clinician when level is approaching side effect? Stop it before side effect occurs? Would this stop before they got therapeutic benefit? Balance. Drug might get into system quickly but damages cells over a week or so?

Scientific challenges /opportunities



- Modelling to avoid harmful effect. Could be patient diary providing data.
- Chemo blanket over a period with high toxicity. How much chemo has worked – don't need 6 sessions as it's worked/not working
- Machine learning to take into account toxicity in body. Can train the data based on population
- Would you benefit from lymphatic imaging – yes. It is possible. Lymph packet transport in the skin. Opto acoustics distinguishes tumour from skin. Can go centimetres deep. Guide optical fibre to the place.
- Sensing going from the ward to the home. If patients know what they're being asked – usually good at filling in. Wireless/implanted – just need their consent to do it. Happens already with heart monitoring. Only if non-invasive – need to get them on side.
- Smart drugs – synthetic biology. Can you release diff drugs depending on what you detect? Released in hypoxia/ or in a system where immune system suppressed. Hydrogels.

Scientific challenges /opportunities



- Traditional chemo – higher dose the more cancer cells you kill. Blood count monitored to ensure not too much. Newer targeted drugs, not necessarily higher= better. Dosage variable.
- 3D model in chamber – growing spheroids. Dosage testing to see how much you need.
- If they're responding well, may want to increase dosage
- Cancers can become resistant to drugs. Can you do intermittent dosing. Measure. Stop. Re-treat. Competition between cells for space/resources. If you take out just one type of cell, you lose that competition between sub-population of cells. Can you detect resistance? Personalise.
- Is there advantage to understanding spacing between treatment and observations? Only empirical in cancer to date.



Scientific challenges

- PDX – patient derived xenographs – grow it, can we predict response? Too hard. Haven't been good at predicting yet. Is there potential to have in-vitro test to give more information? Would need to be very sophisticated. Could you grow it in a bio-reactor? Stimulant hasn't been right yet. Immune cells. Scaffold tech and tissue eng has scope to exploit. Might help design treatment (not for that patient) Patient themselves is ideal bio-reactor. They have to volunteer. Needs to be very well informed.
- Would like to measure everything – put in a chip that measures everything. What do you want to measure? Secreted cytokines(?) in blood. Don't know if there are other things in their urine that will give info. Need to work out what the markers are.
- Can transmit data from implantable. Pacemakers have this already.
- What's happening in the tumour is dynamic.
- Immunotherapy has a lot of focus currently.
- Chromotherapy – not sure where this has got to? Give treatment at diff time of day for each patient. Sleeping pattern, metabolic levels etc Not known how this all fits together and how to use this to make a decision. Still a valid question.
- Cycles of measurements. You may happen to come into clinic with a 'bad' reading, when it's been different previously. If you had more continuous measurements you could

Potential projects

- Broader than chemo?
- When you're learning how a drug works, having measurements to see how things behave.
- CT, MRI and FTG-PET are used. No optical sensors used. The physics doesn't work as the light won't transmit. Could you learn things about the lump through sensor? Implanting a chip might be feasible that measure things. There are materials that could detect interesting changes in tumour. Optical signal converted to electrical signals? Molecules detected would help decide treatment.
- VOC Volatile organic compounds – can measure in urine/breath

Potential projects

- Radio therapeutics more targeted. Yes focus on this for more localised tumours. Eg prostate, lung. Implant radioactive beads. Put in a probe to measure.
- Modelling to prevent resistance – sensors crucial to work out what's going on in patients. Measuring cell-free DNA. (DNA that's not in a cell. If a cell dies DNA enters circulation so you can tell what cells are being killed by drug. If you no longer see that, indicative of resistance.)
- In-vitro, in silico, animal modelling
- Engaging patients better – linked to implantable/ devices, smart release tools. Alleviating hypoxia

Potential projects

- How quickly could you know if this patient responds to this drug? In clinic you'd do 8-12 weeks resolution now. What could we reduce this to? What do we measure? At the mo, size. Growing, stable? What could you measure not in hospital? (home?) Some treatments the tumour gets bigger before it goes smaller. What other indicators apart from size will tell you if it's working? Lots of cancer researchers trying to find surrogate markers. Not necessarily using smart materials. They are using biological.
- Breath analysis – blow into balloon. VOCs. Screening a lot of people to see if differences. Lung cancer – busy signal. Challenging. Diagnostics possible. Some cancers – bladder, can see stage by what VOCs in urine. Some drugs metabolise differently. Sputum, saliva. Can see breakdown of the drug. Not been exploited yet. New. Few longitudinal studies done.
- Patient in the feedback loop. Better info. Patient wants to do it.