Application for the RDSYH Public Involvement in Grant Applications Funding Award – Call 8 - Matthew Marzetti (Novel Applications for Sarcoma Assessment - NASA)

Introduction

Public involvement funds were requested to support the development of an NIHR doctoral fellowship application. The proposed project aims to improve the diagnostic accuracy of MRI for soft tissue sarcomas. Soft tissue sarcomas are a rare type of cancer that can occur in any part of the body that contains soft tissue, for example muscles, fat or nerves. There are lots of different type of sarcoma, which can look and behave very differently from each other. While soft tissue sarcomas are a rare type of tumour, soft tissue masses and lumps are very common. Benign, or not cancerous, soft tissue lumps outnumber cancerous ones by 100 to 1. The time waiting for a new lump to get checked to see if it is a cancer or not can be a very anxious and worrying time for patients.

Magnetic resonance imaging (MRI) is the best type of imaging available to tell if a lump is a sarcoma or if it is benign. Almost all patients who might have a sarcoma will have at least one MRI scan. Unfortunately, sarcomas and benign lumps can look very similar on MRI images. This means that telling the difference between them only using images is hard. Because it is difficult to tell which lumps are sarcomas, most patients need to have a soft tissue biopsy. This is when a small amount of tissue is removed from the lump so it can be looked at in a lab. Having a biopsy means patients need to make an extra trip to the hospital, and it can be painful. There may also be a long time between having the biopsy and receiving the results. Because it is difficult to tell which patients have sarcomas using images only, a lot of patients that do not have sarcomas will have painful biopsies. This also means that waiting lists can be very long.

This project aims to use a combination of MRI and artificial intelligence (AI) to try and improve both the accuracy and speed of diagnosis of soft tissue sarcomas to allow them to be detected earlier.

This project has previously been discussed with an oncology public and patient involvement group. While this meeting was useful and participants were very supportive of the project and its goals, it was noted that only a single members of that group was affected by soft tissue sarcomas. This member was recruited by the researchers specifically to give feedback on this project and was not an existing member of the focus group.

It was felt that a wider range of opinions and experiences of those most affected by sarcomas would be beneficial in the development of the project. Due to the rarity of this condition, no established public and patient involvement groups were known locally. As such, the funding awarded by the Research Design Service in Yorkshire and Humber was used to establish focus groups made up of those who had previously suffered from sarcomas, or who are currently being treated for sarcomas.

Aim

The aim of the award was to find and engage with a group of patients that could feedback on the proposed research project and provide suggestions and opinions on the direction of the research.

Method

In order to recruit those affected by sarcoma the researchers collaborated with the charity Sarcoma UK to find interested people affected by sarcoma. Initially an online survey and information leaflet was developed, which was shared by Sarcoma UK on their social media channels and in their newsletters.

The survey asked questions about how willing patients would be willing to remain in the MRI scanner for a bit longer to gather extra information if it could improve the speed or accuracy of their diagnosis or replace biopsy. They were also asked questions relating to how acceptable they would find the use of AI in their diagnosis.

As part of this survey patients were asked to leave their contact details if they were happy to discuss the project further. Ninety-one people responded to the survey, with 37 leaving contact details and wishing to get further involved.

Emails were sent to these 37 potential participants to discuss how they would like to be further involved. Fifteen participants wished to take part in an online focus group, while a further three opted to take part in individual conversation over the phone. Due to the participants being based all over the country and the on-going covid-19 pandemic all patient and public involvement (PPI) activity was carried out either online or over the phone. Nurses at the Leeds Sarcoma Centre were also contacted to try and recruit current, local patients, however only one patient was recruited this way.

All focus groups were carried out over Zoom, with the support of Amy Rebane, Patient and Public Involvement/Engagement Manager, at the Leeds Biomedical Research Centre. Each focus group meeting lasted for approximately one hour, although 90 minutes was booked to ensure that no one would get cut off if they still had more to say. One focus group was carried out during working hours (1:30- 3:00 pm on Monday), and second one in the evening (6:30 - 8:00 pm). These times were agreed with participants in advance to ensure that all could attend. Unfortunately, due to last minute work or personal issues, or technical issues, three patients had to drop out of focus group meetings. All of these patients have been offered onto-to-one conversations with the researcher, although to date none have followed up on this offer.

Individual conversations happened over the phone, at the request of the patients. These were agreed to be at a mutually convenient time between the researcher and the participant. These lasted between 15 and 30 minutes.

Evaluation of PPI activities

Survey

Survey results were analysed prior to starting the focus groups. In questions where multiple choice options were given the percentage of respondents for each answer was looked at. The comments for those who chose to write their own answer or expand on the options were also reviewed. The answers by respondents who were more cautious about the research were particularly carefully reviewed in order to try and understand their concerns.

In text questions a word cloud was generated to highlight common themes based on how many times a word was mentioned. Areas highlighted by several respondents as being areas of concern or where they would want more information where chosen for discussion in the focus groups.

All responses have been saved in an excel format and graphs plotted where appropriate.

Focus group

Both focus groups were recorded and transcribed (with permission from the participants). These were stored on a secure network drive, and were only accessible to the researchers. The recordings and transcripts were used to create detailed notes of the conversation. Recording the focus group allowed the researchers to focus on the conversation at the time rather than having to take notes.

Key themes and points were identified from across the two meetings. These were recorded in an impact log. These key points and associated actions were emailed to all participants to make them aware of how their work has influenced the project.

Participants were sent a survey to complete to comment on their involvement. This will be reviewed once more of the participants have had a chance to reflect and respond to the survey. This will allow the research team to make changes to how PPI activities are conducted based around patient feedback.

Telephone conversations

Notes were taken during telephone conversations. A quick background to the project was given to the participant at the start of the call, after which they were given a chance to ask any questions or give any comment. Following on from this the researchers asked questions around the same topics as those used in the focus group. The individuals answers to the survey were also analysed to ensure anything they had mentioned in the comments was picked up in the conversation if appropriate.

Patient account

Awaiting reply - 2 patients have said they will do this however I have yet to receive it.

Results and Outcomes

Survey

Results from the survey were overwhelmingly supportive of the project. All respondents bar one, would be happy to remain longer in the MRI scanner to either improve accuracy and speed of diagnosis or replace biopsy. It should be noted that the only patient that was unwilling to have an MRI has a pacemaker that is not safe for MRI. This has raised questions about access for those patients with MR unsafe implants.

Some respondents flagged that they have been misdiagnosed from MRI scans before and in some cases not sent onwards to biopsy. In some cases this was used to support the research - if the AI algorithm detects sarcoma more accurately than a human they would have been treated sooner - whereas other respondents were more cautious about replacing biopsy completely.

There was a lot more hesitancy surrounding the use of AI in making a diagnosis. Seventy four per cent of respondents were comfortable with an AI algorithm helping their clinician make a decision about their health care, but only 11% would be happy to let an algorithm make the decision alone. A further 15% would want more information or convincing before letting an AI algorithm have any part in their healthcare.

Topics that elicited more divisive responses during the survey, such as hesitancy to include AI in healthcare, were used as topics to guide the focus groups.

Focus group

The response from the focus group was supportive of the project. Participants were initially given a presentation on the proposed research and invited to feed back their opinions on it. Generally the project was widely seen as being valuable and contributors were supportive of methods to speed up and improve diagnosis. Even among participants that were claustrophobic, it was felt that for a fast and accurate diagnosis spending a bit more time in the MRI scanner would be ok. All patients were fairly comfortable with the idea of their images being used anonymously for research, including by researchers in the NHS, at a University or healthcare researchers in Europe.

Several patients shared their personal stories and highlighted where this algorithm could have been beneficial. This was particularly the case in which radiologists had looked at their scans and not referred them on to specialist sarcoma services as the lump wasn't thought to be malignant. However, several patients raised concerns about the more advanced MRI techniques, and whether these would be available in their local hospitals or only in the more specialised ones. These are valid concerns, and would limit the utility of the proposed research to only those hospitals with access to more advanced scanners and patients referred on to specialist sarcoma services. As a result it has been proposed that an artificial algorithm should be developed using only the most basic images, which can be acquired routinely on all MRI scanners. This will be incorporated into the project. The literature suggests that this can still help improve diagnostic accuracy. This project will seek to develop two separate AI models, one that will work with routinely acquired images, and a separate one using more advanced images. If the diagnostic accuracy is high enough, then the models generated by this project will be able to be used more widely.

Another key point mentioned by some patients was that they would be reluctant to give up biopsies. This was particularly prevalent in public contributors who had been misdiagnosed by imaging in the past. This point was discussed in both focus groups and it was agreed that a period testing the algorithm in a "real-life" situation would help convince patients that it was safe to use. During this testing period the results of the algorithm would not be influencing anyone's care, however results would be collected and compared to the final diagnosis to measure accuracy. While this was always part of the project idea, it will be communicated much better to patients in the future.

One of the PPI participants, who works as a computer scientist, was keen to suggest that focusing on one metric for measuring accuracy to really highlighting the models performance was a key way to convince people of its utility. This participant has agreed to be contacted as the project development continues, to give his input on how best to communicate results to patients. It was also suggested that getting a big technology company on board could help, as well as getting anything endorsed by medical groups or charities such as Sarcoma UK. It was suggested by both focus groups that I keep working with Sarcoma UK to communicate with patients. The researchers intend to remain in contact with Sarcoma UK throughout the project.

A final point that many patients mentioned was that they found it a "battle" to get scans and were often dismissed when first visiting their GP. It was rightly pointed out that if patients can't access MRI, then this project will not be able to help as it requires MRI images. This is a valid point and requires awareness of sarcomas to increase, as they are a

very rare condition. We will endeavour to raise awareness through this research wherever possible. Furthermore it may be that if this project is successful then patients are more likely to be referred for MRI given that there will be clinically validated tool to make a quick diagnosis from the images available. However this is a point which the research team will need to consider more fully as it is something we have been unaware of until this point. One option may be to use other imaging modalities and not just MRI, however MRI shows most promise at present for diagnosing sarcomas accurately. If we are successful with MRI we would look to expand the project to include other imaging modalities.

Costings and compensation

There was no compensation for completing the survey. However, following on from the survey, respondents were offered a £30 Amazon voucher for participating in a focus group, or £10 for participating in a phone conversation.

The compensation for participating in the focus group was reduced from the £50 specified in the application for funds to £30. This was done because significantly more people left contact details in the survey that was expected (37 as opposed to 15-20). It was felt it would be better to include as many people as possible, so to do this and offer equal compensation to everyone, the compensation had to be lowered. To compensate for this focus groups were shortened from 1.5 hours to 1 hour so that they were not as big a time investment for the patients.

Fifteen patients signed up for focus groups, which would have cost £450. However three then had to drop out last minute, and a further three turned down the vouchers, meaning focus group costs of only £270 were incurred. A further £20 was spent to compensate two patients for their time discussing the project on the phone (£10 per patient). A third patient turned down compensation.

Future work and discussion

Each patient was asked either during focus groups or during individual conversations if they would like to stay in touch as the project develops. All patients agreed to be contacted in the future and to stay in touch. A summary of the focus group meetings has been sent out to all participants.

If the work is awarded funding, a patient steering group will be formed. Participants of the focus groups supported by the grant will be invited to participate in the steering group. Furthermore, funding will be requested as part of the application to have at least two focus groups a year. Participants of these two initial focus groups will be invited to be part of future focus groups during the application, however new participants will also be welcome.

In retrospect there are several areas in which this activity could have been improved. The first of these deals with the recruitment of participants. Participants were for the most part recruited through a partnership with a charity that focuses on sarcomas, Sarcoma UK. This was done as sarcomas are a relatively rare diagnosis, and it was challenging to find a large pool of patients. However it is recognised that given this project proposes using artificial intelligence techniques to help diagnose sarcomas, that by recruiting participants digitally there is a potential to bias the focus group to include those patients more comfortable and familiar with digital technologies. An effort was made to recruit patients

through the Leeds Sarcoma Centre as suggested by the RDS awards panel, however this was challenging due to the on-going Covid-19 pandemic. More patients will be approached in person during their treatment for future focus groups.

A second area which could be improved includes the paying out of compensation to patients. Compensation vouchers were only requested through the NHS system after the focus groups took place, as researchers were assured this would be a quick process and did not want to order too many. However, there has been a long delay in getting these processed by finance, which is unfair on the participants, and resulted in a 2 week wait. In future compensation vouchers will be requested well in advance of any focus group meetings.

The lead researcher had very limited experience working with members of the public and patient prior to working on this grant. As a result they were unaware of the likely number of patients to sign up to events, or the numbers that are likely to drop out or decline compensation. Costings for reimbursement could have been planned better had the researcher been more familiar with the process. A great deal of learning has taken place for the researcher as a result of this grant, including making contacts with the PPI team at the Leeds BRC. It is felt that future PPI work will proceed more smoothly as a result of the experience gained carrying out this work.

The project that this PPI work has helped support and develop will be submitted as NIHR clinical doctoral research fellowship application in April 2022, with an expected start date of April 2023 if it is successful. PPI will be built into the application and costed for accordingly.

Acknowledgements

As well as the thanking the RDS Yorkshire and Humber for making funds available, the researchers would like to thank Sarcoma UK for promoting the research on their social media channels and connecting the researchers with patients. We would also like to thank Amy Rebane, Patient and Public Involvement/Engagement Manager, NIHR Leeds Biomedical Research Centre (BRC) for her extensive help in setting up and running the focus groups, as well as her advice on how to get the best from the meetings.

We would also like to thank Holly Schofield for her help and advice both while applying for the award and while conducting PPI activities.

Appendix A - detailed breakdown of how the funding was spent

Item	Number	Cost per unit	Total cost
£30 Amazon voucher - focus group compensation	9	£30	£270
£10 Amazon voucher - one-to-one phone call compensation	2	£10	£20
Total			**£290**

Appendix B - feedback from participating members of the public

Participant 1

I recently took part in patient and public involvement activities carried out by Matthew Marzetti about his proposed research looking at new ways to diagnose sarcomas using artificial intelligence and MRI.
My interest comes since my primary Sarcoma diagnosis in my right thigh in 2019. As part of diagnosis I had a lower body MRI scan and had to wait some weeks for confirmation as there was a real limitation on who could review the scans, being under a small NHS trust, here in Cornwall.
Should a full body MRI, or even just the lower body MRI, the AI detection method could have saved in confirmation the diagnosis and given confidence in further disease progression elsewhere.
I first completed an online survey in June, which I first saw advertised by Sarcoma UK on Facebook.
The survey was suitably in-depth, without making it so involved that I felt bored and didn't complete it.
There was information on the project, as well as the next steps in the research. After this I was contacted by the researchers in July, who asked me to be part of a focus group. The focus group was in mid-August, 2021.
I felt it a worthwhile and interesting experience for me; being able to contribute and 'give back' to the medical profession in some small way. It was also good to speak to, and listen to others in similar circumstances to my own. Coming from the Engineering industry, it was really interesting to hear the information on how AI technology could be implemented to improve the standard pathway for diagnosis.
The information was presented well and 'pitched' at a good level, ensuring the research group understood, without needing any significant prior knowledge of the technology.
The research team were respectful of our diagnoses and of the issues we face when living with Cancer.
Each contributor was given time to provide as much or as little of their 'story' as they felt comfortable in sharing with the group, as well as ample and respectful time during responses to Q&As.
I felt that my contributions were noted, worthy and taken onboard.
I would be more than happy to take part in further discussion in research groups for this same topic, or on different projects… so hopefully this says it all on whether or not I thought this session was well ran!

Participant 2

I took part in patient and public involvement activities carried out by Matthew Marzetti about his proposed research looking at new ways to diagnose sarcomas using artificial intelligence and MRI.

I started to become ill in late July as I was waking up at night in excruciating pain. It was as if an elephant was sat on my spine and I couldn't move. I was also experiencing pain on my left side and it was also difficult to breathe. I telephoned my GP on Friday saw my GP who looked at my stomach and tested for ascites, also made referral for ultrasound. The ultrasound showed a mass with a region of "shadow" that we now know were the well-diff and de-diff regions. Referred for CT, although we did speak to BUPA to make them aware and they immediately booked an appointment with a GI consultant who arranged CT at his first appointment, he diagnosed it was likely a retroperitoneal liposarcoma and referred me to a Sarcoma surgical oncologist. After initial consultation where he showed me the CT images of my 38x28x16cm tumour (est mass 10kg) which had enveloped my right kidney, he arranged for a percutaneous biopsy on 9th September. The biopsy showed it was a high grade tumour, largely homogenous but with regions of de differentiation.

On 1 October, the tumour was resected en mass with right kidney, right adrenal gland, right colon, large section of diaphragm and psoas fascia muscle to achieve margin.

In January 2021, I had a surveillance CT scan which unfortunately showed that I had a local recurrence of RPS with metastatic disease in my lungs.

I started chemotherapy (doxorubicin and ifosfamide) in February 2021, concluding in June 2021. My lung mets responded well to the chemotherapy, however the paraspinal lesion grew during the chemotherapy.

I've just completed a series of stereotactic ablative radiotherapy on the paraspinal lesion. Once recovered from SABR, there will be further surveillance CT on the lung mets to determine further treatment approaches.

Thinking about this study and my patient experience, I would make the following observations:
- Logically, the study would use machine learning based on multiple sets of real patient data. Given the rarity of STS, will there be enough data to build a reliable model? Does the study need to seek data sharing from other Sarcoma centres to build the AI?

- For AI to be adopted as a viable diagnostic alternative to biopsy, the AI must be able to achieve the same diagnosis as would have been reached through the biopsy. With my diagnosis, there was a CT of my abdomen that showed the retroperitoneal liposarcoma with a "95% confidence" from my surgeon, however a biopsy was required to confirm it was RPLS. On that basis, I would expect that the machine

learning that drives the AI is matched to achieve a 100% correlation between AI diagnosis and biopsy diagnosis in the test data.

What could be a good avenue for the AI is whether you can diagnose from possible past missed diagnosis e.g. I've heard a surgical oncologist talk about cases of sarcoma which were misdiagnosed as cervical cancer. The dedifferentiated regions were resected, believed to be "the tumour" only for the patient to still have the well-differentiated region left behind as "healthy tissue" - could the AI spot for sarcoma where it might not have been considered?

- One of the reasons given for my biopsy was to determine/confirm whether it was dedifferentiated. Will the AI be able to determine differentiation?

First I completed an online survey in June, which was advertised by Sarcoma UK on Facebook. The survey asked the right amount of questions and I do not remember it being cumbersome to answer. After this I was contacted by the researchers in July, who asked me to be part of a focus group. The focus group was in mid-August, 2021.

The focus group was well organised with introductions from all the researchers and participants. The explanation of the proposed study was given and then the participants were free to ask questions either by writing on the message system or by putting their hand up physically or on the hand icon on Zoom. The participants asked questions and interrogated the information that the researchers had given to the focus group and how they potentially would have been impacted by the study if it came to fruition.

The focus group was well planned by the researchers and I everyone was able to have their questions answered.

Hopefully the AI will be developed that is 100% effective at diagnosing sarcoma, without the need for patients to undergo painful biopsies.

Good Luck with the research.