OsStic: An Adhesive Technology for Ortho and Beyond

Philip Procter, CEO of GPBio & co-founder of Biomimetic Innovations, shares the OsStic journey of discovery and its path to commercialization in an interview with SmartTRAK

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Philip Procter, CEO of GPBio & Co-Founder of Biomimetic Innovations started on a quest several decades ago to solve trauma hardware failure in patients through the development of an adhesive solution. The journey began in earnest after a UK meeting with craniomaxillofacial surgeons facing difficult problems they felt could only be solved with an adhesive technology in combination with implants. Procter was convinced early on that the adhesive solution would have to come from nature studying everything from gecko-based technology to sticky frogs in Australia to Mytilus edulis (common mussel) food protein. But it was after demonstrating the potential of a prototype glue in Sweden in 2014 (see Figure 1) that his journey led him to become a faculty member of the University of Uppsala, Sweden, and he and his partner Dr Gerard Insley working together with Professor Håkan Engqvist and a team of students developed the technology that is known today as OsStic: a technology with the potential to join implant to bone, bone to bone, soft tissue to bone, and soft tissue to soft tissue.

GPBio and PBC Biomed, both Irish-based companies, joined forces in 2020 to develop and commercialize the OsStic bone adhesive technology through the formation of a new company, Biomimetic Innovations Ltd. Company CEO Philip Procter shared more about the OsStic technology, how it came about and next steps for bringing the product to market in an interview with SmartTRAK's Lisa Mahan. To listen to the interview, visit https://vimeo.com/636761675.

SmartTRAK: Can you give us an overview of the OsStic technology?

Philip Procter: So what is OsStic like? It's like making a souffle, really simple ingredients, but to get a great souffle you have to know what to do with the ingredients, it's the same with the adhesive. It's water, it's calcium and a simple amino acid, a non-essential amino acid called phosphoserine. And it's this amino acid that sea creatures such as mussels use to make their connection to surfaces underwater. It was the presence of phosphoserine that turns out to be an attractor to an enormous range of surfaces. Eventually, I figured out that what was going on in mussels sticking to things was also linked to the presence of phosphoserine in humans.

Figure 1.

Early demonstration of potential as bone-to-bone adhesive

By chance, one of my PhD students in Switzerland had a substitute professor step in to do her doctoral exam. And this man, who'd been in America, Professor Georg Fantner sat next to me after her thesis presentation. And I say, 'Professor Fantner, what's the burning research that you're working on at the moment?' And Professor Fantner, says, 'oh, we have found this really unusual mechanism in human tissues related to collagen that appears to be part of a reversible glue mechanism involving a material called phosphoserine.'

So I'm now really intrigued, but I'm also reassured that when this goes into a human being, after it goes through the first animal tests, we have a chance of showing compatibility. It could be a material that is as natural to us as all the other materials that we know that the human being is made of. So can we prove that it's safe? So we do an animal study. It's in small rodents. This shows that the material is entirely benign and safe, but now we need a model to prove it's effective as a bone glue.

The end of this story is we become incredibly proficient at removing a small core of bone that we can then reliably reposition with the adhesive in the live animals. And this enables us, at different time points after implantation, to chart both the histology and the physical strength throughout the course of healing.

You said that the first application that you're looking for is you're going to take it and do bone to bone. So looking at more trauma applications, is that correct?

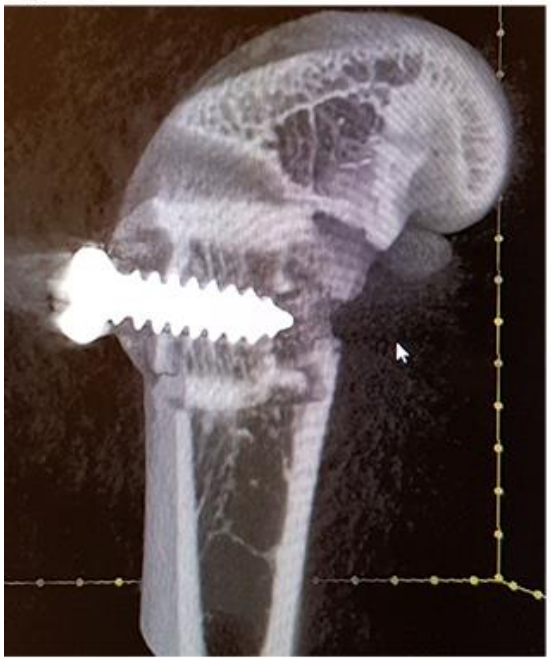
PP: I think the honest answer to that question is first we need to explain the commercial side of things. We had a little company called GPBio that Gerard [Gerard Insley, GPBIO co-founder] and I had formed to create IP in a contained way that later could be transferred to anybody who wanted to acquire it. So, in February last year we also formed a company called Biomimetic Innovations. And Biomimetic Innovations has the goal to commercialize the applications based on GPBio's IP. And the primary fields of application broadly are everything in the human body around bone, where you're using screws and plates and conventional implant hardware.

Why do we see lots of applications there? It's because of the poor quality of bone in older patients. When you glue a screw in place, you get a fixation strength that's extremely high compared to any other method, even comparable to polymethyl methacrylate which is never going to be integrated into the human body. The real interest is osteochondral bone fragments. When you smash your knee, when you smash your elbow, when you fall over and smash your wrist, yes you can pull the big fragments together with screws and plates. BUT you have small pieces of articular surface that you cannot fix with the kinds of screws and hardware that we have. So to visualize how this works, imagine you've got your favorite china cup and it's fallen and broken into 10 pieces. Four of those pieces are very big and you've got six small fragments. Ideally, you glue together the small fragments to make a couple of big pieces alongside the other big pieces that you've got.

That's the kind of approach. And if you would ensure that the joint surface is maintained during the healing, then this gives the cartilage at least a chance to heal to some degree. But more importantly, it means there's no discontinuity in the joint surface. And you could imagine a mechanical bearing surface might heal with a surface discontinuity. And that's the issue that leads eventually to post-traumatic arthritis. So if you don't fix the knee joint perfectly, what's going to happen is they're going to need a total knee joint after a period of time. So it's really those two big areas I would say in the orthopedic part. In soft tissue, I would lose count of the different ways it might be useful. If you think of all the soft tissue specialty areas for instance you have hernia meshes, you have many internal devices where the fixation is sutures.

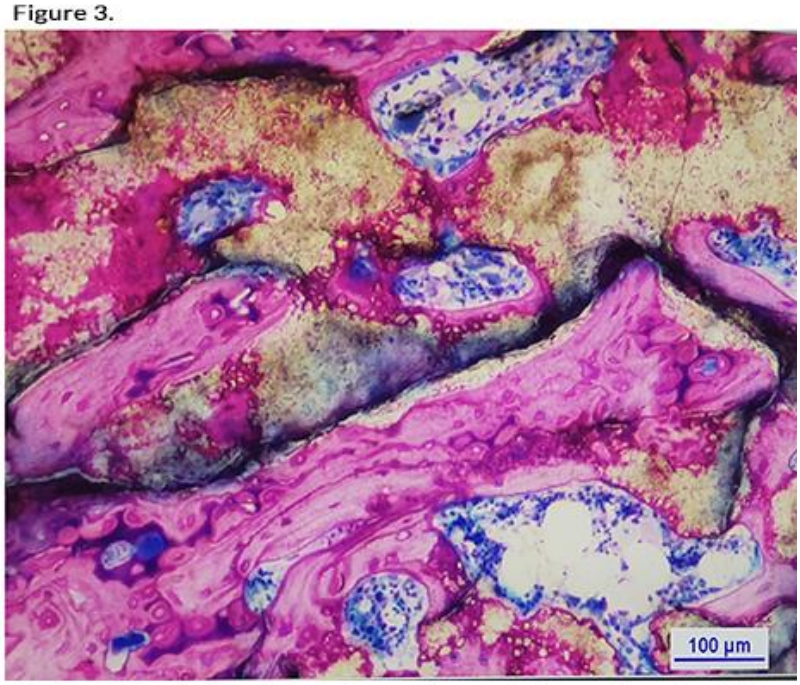
So can you replace the suture in part with gluing? If you have a knee meniscus that you want to repair and you're going to put eight stitches into it, maybe in combination with the glue you only have to use four now. So it's an area that certainly will play out to have many, many applications, but obviously, we come from the orthopedic field. That's where we start. And the other area, which we've become very much involved with now and interested in is the dental field. There's a lot of possibilities for dental procedures to be augmented. So again, it's augmenting current procedures. It's adding a component that has the ability to really bond things.

Figure 2.



Adhesive testing in a rat bone model

Figure 3.



Histology at 28 days showing residual adhesive converting to good quality cancellous and cortical bone

What's the healing time? Do you have any data or an estimate on what the healing time is after you would use OsStic?

PP: Well, we don't have any human data. We have the first funded project to move forward, to create the first product that will be used in humans. But if we go back to the rat model that we developed, at 42 days 70% of the spongy cancellous bone adhesive had converted to the same bone, the same quality that was there originally. And in the cortical shell they had about 50%. Conversion at 42 days. And outside of the bone envelope, the adhesive was being digested and removed without any excess bone formation. (See Figures 2, 3.) So if we take that as a guide, first of all, there's no ordinary calcium-based biomaterial that will metabolize that fast. The second thing is if you would look at rat days versus human days so maybe it's three to one. And if at 42 days you can get 70% of the material remodeled into good cancellous bone, you could be looking at 120 days to have the equivalent in humans, which is fast. This has to be proven out of course. With the presence of the OsStic, which we feel is strongly bioactive, you could expect much less than 120 days. I'm thinking it could be eight to twelve weeks where you have the right circumstances. So it could really augment the healing process.

You said you have a funded project for commercializing the first product or developing the first product? Is that something you can share?

PP: I can't share this because it's not public domain and we don't have permission to do that. All I can tell you is that it's a leading company that has a significant implant business. We found a serious partner who has the vision and the means to drive this from great laboratory work, into being the first approved product. Right the way through the process of submitting to the necessary authorities. So this will be CE marking in Europe and it'll go through a pre-submission process in the United States and be put in front of the FDA when the necessary work has been done.

So can you share, even if it's high level, what the first commercialization product will look like, is it a trauma product? What area is it in?

PP: I can't do that because of confidentiality.

But it's more in the area of orthopedics? I know we talked before that there could even be applications for heart surgery or other surgeries.

PP: It will be in the skeleton. It'll be about enhanced fixation. Augmented fixation is really a great starting place. For lots of reasons, augmented fixation means that you can either use smaller implants or you could load the implants earlier. So it could mean quicker rehabilitation. And augmented fixation is an area that we have specialized in. We got the first approvals in Europe, by the way, back in 2008 for the combination of a calcium phosphate cement together with a metal implant. And one of our team, one of the great men of American surgical history, got the first FDA approval for a similar combination. So we've got really forward-looking qualified people in our team.

So yes, that's going to be the first area. And if we can also get it into osteochondral fragments it will be great, but it is asking a lot for the world to believe we can glue pieces of bone together with not much adhesive material. (Figure 4)

Figure 4

Dr. Alicja Bojan simulates fractures to evaluate OsStic performance on human cadaver bone

You talked about the regulatory pathway. What are the requirements for bringing this to market? What do you have to go through to get it approved?

PP: Well, the good news is that it's easily qualified as a void filler because that's what essentially, it's doing. It's void filling the spaces between implant and bone. Its additionally bonding both to the bone and implant surfaces in a way that gives much greater fixation integrity. The way that the regulatory world is going, we will probably have to prove out application by application. Imagine we provide something that looks like a glue. It will have to be extremely carefully set up and managed in the clinical setting to make sure that use is correct and on-label.

Are there other bone glues that are already on the market or bone adhesives?

PP: Nope. Zero. We have one competitive group who we used to work with in Stryker. They're making some preclinical progress and it's always good to have a competitor there. But I would say that we have only really that one competitor that we can benchmark against in the class of materials that we're working with.

How does Royal DSM factor into the picture? Do they manufacture the material or how are they part of the picture?

PP: Well, we have a partnership agreement with them and I cannot give you any details of that. It's a strategic alliance in which both parties are looking at biomaterials. We've known DSM for many, many years. And the hope is that for one of the biomaterials that our group is working with, that they would become a partner. The adhesive materials which are currently being used are being handled by us. We don't have any other manufacturer involved yet.

You talked before about some research that just was getting published. Can you go over that?

PP: When I met my former boss last night I said, 'Bernd, I finally have the evidence that you were asking for. We know that this material lets the bone heal. It never lets go of what it's joined to, and the bone reaches through it to join bone on the other side. Basic multi-cellular units are formed deep inside the material, blood vessels form, all the normal bone formation processes occur.' And the histopathologist who's from NAMSA said 'bone thinks this is bone. There's no inflammatory response. Every sign is that normal bone healing is occurring and then it's disappearing. It's like a piece of magic.' So what this project demonstrates is that the adhesive seems to be doing the impossible thing. And the impossible thing is that it's not only safe, it's also effective. It allows healing through itself and then it disappears.

And this is something that's never been seen before in such an early time sequence in healing bone. There are other studies out there that show this class of materials after six months or twelve months. But remember for trauma surgeons, they're interested in how strongly is it joined

together at the surgery. Their questions are: 'At 15 minutes, you tell me it's set. Can I let go then? And yes, there's a decrease in strength, does it fall apart then? Will it become bone when healed? Do I have to do a second surgery?' So this paper is the first real answer to those questions, the first real evidence. Now, of course, it's a new model, it's all new. What we need now is other researchers to test this thinking, to be able to look at it critically and find out for themselves, is it real?

In the world of metal implants, metal almost always works. And now you've got this white sticky stuff in combination with metal implants, and you're telling us it's safe. So what this piece of work does is it lights the fuse on the bigger projects. So, okay, great in rats. What about large animals? That's the next question. Well, we actually have the histology results at one month and three months in pigs. I can't give you any detail of that because done by a partner company. But we know from this, that the same basic cellular behavior seen in the rat is mirrored in a big animal. And then the next question is what about human beings? Well, that obviously is the next logical step. And this is where my hope is that surgeons like my partner Dr. Alicja Bojan and others are now going to do the work necessary to ensure that it's safe and effective in treating human bone conditions.

So if you were predicting, how long do you think it would be before we see the first product on the market?

PP: The very first product that I know of, I think will be in the market in three years.

And what would you like to see as the next indication after that?

PP: So when I say the next indication, if enhanced augmented fixation of implants is the first area, then what I would hope we can do next is to really prove out the osteochondral fragment problem, which is where you're going to probably have less hardware, and perhaps even in some cases, no hardware, because small bone fragments are going to get joined together. I think for me, this would be the icing on the cake. If just those two things existed, this would already give surgeons a far greater control in clinical situations that aren't easily resolved because of poor bone quality and how badly a bone can be broken.

I thank you for taking the time today. I think this is fascinating. This is a concept that you've been working on for how long?

PP: Maybe 30 years. And I think I might've told you about Arthur C. Clarke. This is the guy that wrote the 2001 Space Odyssey and was so influential in thinking about science-fiction. And he just wrote this very simple thing about technology that 'any sufficiently advanced technology is

indistinguishable from magic,' the corollary being if a technology does not look like magic it is not sufficiently advanced. In some small way with OsStic I have converted science fiction into a science fact. And I was privileged to be present at the moment it happened. That's a fantastic buzz. I still can't believe that we've finally got the publication accepted. And as I re-read it I thought, 'Did I write all this? Did we really do all this painstaking work?' It's really funny to think I wrote over 130 versions of this. And it was only the last 10 or so where it suddenly becomes the story that it is magic.

Well, thank you.

PP: Thank you for the invitation.

Thank you.