Transcript Details

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Cardiology Among the Constellations: Exploring Microgravity & Space Flight

Dr. Brown:
Space travel has long-enthralled the minds of many. And healthcare professionals are no exception. And today, we're gonna find out what happened when one asked the question, "How does microgravity affect cardiac function?"

Welcome to *Heart Matters* on ReachMD. I'm Dr. Alan Brown, and joining me to discuss this out-of-the-world topic in research is Dr. Arun Sharma, a stem cell biologist at Cedars-Sinai Medical Center in California. Dr. Sharma is also a host for the Stem Cell Podcast, an internationally recognized podcast that discusses advances in stem cell biology. Dr. Sharma, welcome to the program.

Dr. Sharma:
Thank you so much for having me.

Dr. Brown:
To start us off, Dr. Sharma, can you tell us what we currently know about the effects of space flight on the heart?

Dr. Sharma:
There have been a number of studies that have occurred over the past decade, since astronauts and mankind have been spending time in space, or the International Space Station, and elsewhere. We have an understanding of what happens at the bodily level when it comes to the impact of low gravity and space flight on cardiac function. Just as a brief overview, we know that the heart itself changes shape a bit during prolonged exposure to low gravity. Typically, as we all know, the heart has somewhat of a fist-shaped structure, but in orbit and in low gravity, over extended periods of time, it can actually restructure itself to more of a spherical shape. And in part, that has to do with the fact that there's a reduction in overall load that the heart is actually experiencing. A major portion of what you and I are experiencing here on the planet is the force of gravity, and the force of gravity has a massive impact on how the heart actually functions. In space flight, in low gravity, that force is no longer there, so the heart doesn't necessarily have to work as hard. And because of that, there are some instances of changes in heart rhythm, changes in overall muscle mass, which is, definitely well-documented and in part, to combat some of these changes that are happening in overall cardiac physiology, astronauts have to exercise for hours on end on the space station, just to keep their hearts, their musculature, their skeletal structures healthy during this really, really stressful period of time in extended micro-gravity.

Dr. Brown:
With that being said, can you share what led you and your fellow researchers at the Stanford Cardiovascular Institute to focus on this topic of micro-gravity's effect on the heart cells, specifically?

Dr. Sharma:
Sure. So as I was just describing, there's a compendium of knowledge out there that describes what happens to the entire heart over extended periods of exposure to low gravity and during space flight. But there's less of an understanding actually of what happens to the individual cells of the heart and the individual cells of the other organs of the body during this extended period of exposure to low gravity. And we really wanted to take advantage of a piece of technology that's emerged in the field of stem cell biology that really, for the first time, allows us to mass-produce human heart cells and personalized human heart cells, cardiomyocytes, in vitro, by the billions. So now that we can actually mass-produce these induced pluripotent stem cell-derived myocardial myocytes, we actually wanted to utilize them for studying the effect of low gravity on the individual cells of the human heart.

Dr. Brown:

Now, Dr. Sharma, I'm sure your team did not bring literal heart cells from a patient onto the International Space Station, so how did you get to analyze the micro-gravity effects on heart cells?

Dr. Sharma:
Right. So, you know, the power of induced pluripotent stem cells, you can make a person's own cardiomyocytes from a small sample of their own skin or blood and this reprogramming process takes about a month, so we basically had mass-produced our iPS-derived cardiomyocytes ahead of time and then took those cells, purified those cells, sent them aboard a SpaceX Falcon 9 rocket to the International Space Station for 1 month and actually during that time, they were maintained on orbit actively by an astronaut who is not only an astronaut, but also a cell biologist, Dr. Kate Rubins, and in fact, we are very fortunate to have her as our hands in the sky taking care of our experiment. So with the help of Dr. Rubins, we were able to maintain these cells, conduct weekly nutrient-exchanges on them, conduct functional analyses on cardiomyocyte contractility, preserve samples for downstream RNA sequencing and transcriptomic analysis, and in fact, we also returned a sample of these cells, live, back to the planet, during which time they were actually analyzed further by our laboratory at Stanford University. And we were able to determine a number of functional and structural changes that actually happened at the level of the single cell after long-term exposure to micro-gravity.

Dr. Brown:
So, this is really fascinating. I'm curious about what your hypothesis was? You had some evidence about the intact heart and how it might behave in space, prior to this research, so did you have a hypothesis in mind of what you expected to see on the myocardial cells themselves?

Dr. Sharma:
We did. And our hypothesis was simply that because there's no reduced force of gravity on the space station, these cells would not have to work as hard and they would elicit a lower amount of force at the level of the single cell. So in fact, that's actually what happens to the heart as a whole in orbit. And indeed, that's what we ended up actually observing, these cells not having to contract nearly as hard, certain features related to calcium handling were overall reduced and there were actually changes that happened in gene expression related to metabolic function as well.

Dr. Brown:
So, were you thinking that in addition to the need for less energy expenditure that you might see changes in organalysis like mitochondria or other structural changes in the cell, in addition to a reduced expenditure of energy and force?

Dr. Sharma:
Right. It's a good question. In fact, we were expecting to see a stronger signature of sarcomeric change; the sarcomere is, of course, the contractile machinery of the individual cardiomyocyte. We expected to see a stronger rearrangement and perhaps a down-regulation in the overall sarcomere structure. That's actually one thing that we did not see at at the macro level but we did see a number of these changes at the functional and also at the genetic level, for example, the changes in mitochondrial function.

Dr. Brown:
For those just tuning in, you're listening to *Heart Matters* on ReachMD. I'm Dr. Alan Brown and I'm speaking with Dr. Arun Sharma about his recent study looking into the effect of micro-gravity on cardiac function. So, you started to tell us a little bit about some of your findings; were there other things that surprised you with regard to either functional or structural changes in the cells?

Dr. Sharma:
Well, I think one thing that was surprising was that when we did observe some of these functional changes, such as changes in calcium handling and contractility, for the most part, these changes reverted back to normal when the cells actually returned back to the planet, which is somewhat reassuring, right, if you're an astronaut who's spending an extended amount of time in low-gravity, ideally, you wouldn't want to have those changes in cardiac physiology maintained when you actually returned back to the planet. And at least on the level of the single cells, it does seem that there's a period of time at which those changes are maintained when the cells return back to the planet, but over continued culture ground-side, those changes tend to revert back to "normal" at the level of the single cell.

Dr. Brown:
Yeah, that's really fascinating. Obviously, there are changes in afterload on the heart, so the loading of the heart as an intact heart gets changed, and you're gonna have to educate me on this because I don't know a lot about the evaluation of cardiac function in space, but were similar findings found in the intact heart that when people returned to Earth, there was a remodeling, so to speak, or a reversion back to normal in terms of myocardial contractility and dealing with the increased load on the left ventricle?

Dr. Sharma:
Yes, exactly. So, some of those changes that you're describing at the macro level of the organ, the entire heart, are well-documented

and they have been documented over the last decades, as astronauts have spent time in space aboard the International Space Station, sometimes for periods of months, but for the most part, those changes do revert back to normal when the astronauts return back to the planet. And again, in the parallel fashion, we're seeing that at the single cell level as well.

Dr. Brown:
So, one specific finding that came out of your research was that heart cells can actually atrophy quicker in space versus on Earth and I think we generally think of atrophy as something that's not really significantly reversible, so how long did it take to see the heart cells start to "atrophy" or weaken and then after you got back to Earth, you gave us a little bit of a clue, but roughly how long did it take for things to return back to normal?

Dr. Sharma:
Yes, just to give you an idea of the timeline, some of these structural changes and functional changes that we're observing on orbit happen within the period of days, or really within the first week of the cells actually being cultured on orbit, but the changes that I described revert back to normal within days of actually returning back to terrestrial Earth-side.

Dr. Brown:
So, for my final question on this fascinating topic and it's something that would be fun to talk about for hours: as we anticipate relatively long space flights, for example, going to Mars in the near term and people spending months or maybe years in space travel, do you think that something's going to need to be done to compensate for the effects of zero gravity on the heart or are you fairly confident that even after those long periods of time, our myocardiocytes will be able to return back to normal function?

Dr. Sharma:
It's really the million-dollar question. It takes a few months to actually get from Earth to Mars, right? And the Martian gravity situation is very different from gravity here on Earth, so, even if you're able to land successfully on Mars and establish a colony or research station or something like that, the environment is still very different from the human body has grown accustomed to. Ideally, I think the real dream in this field would be the development of some sort of pharmacological intervention that might be able to mimic, say, extended periods of exercise aboard the space station that these astronauts have to do. If you can pharmacologically maintain cardiac function, skeletal function, muscular function, without, you know, these strenuous activities, then that would be very advantageous, not only for space flight, but those of us here on the planet as well. There are a lot of parallels between what actually happens to the body in low gravity and extended aging, so really, the space flight environment and the changes that it elicits to the body, they're a form of accelerated aging, and so a lot of the parallels that we're seeing there, the gene expression changes, the functional changes, they could really inform aging-related diseases here on the planet. So, I think there's a lot of benefit to be gained from this kind of work.

Dr. Brown:
Well, that's fantastic. Really interesting. I always think of Einstein's theories that we could go out at the speed of light for decades and come back only a few days later, but I would hate to find out that the body aged dramatically during that trip, that would ruin the fun of it

Dr. Brown:
So are there any innovations in terms of potential devices or strategies to maintain muscle function and cardiac function for these long trips and especially trips to places where the gravitational pull might be significantly less?

Dr. Sharma:
Well, the easy way to do it as I described is to continuously exercise and that's what the astronauts are doing. Until we're able to find a way to maintain cellular integrity and physiological integrity of the cardiac system, the cardiovascular system or the musculoskeletal system, I think that's the best we can do right now. And for the most part, it's done quite well, but again, it is the dream to find some sort of pharmacological intervention that would be able to mimic those effects.

Dr. Brown:
Well, with those exciting possibilities on the horizon, I'd like to thank you very much, Dr. Arun Sharma, for joining me to discuss research on microgravity's effect on heart cells. It's an unusual, but fascinating topic. So thanks, again, for being part of it today.

Dr. Sharma:
Thank you for having me.

Dr. Brown:
And if any of our listeners are interested in learning more about the latest stem cell biology research, you can hear it from Dr. Sharma and other leaders in the Stem Cell Podcast. I'm Dr. Alan Brown and to access this and other episodes in our series, visit ReachMD.com/HeartMatters, where you can Be Part of the Knowledge. Thanks for listening.