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00:06 Sarah Crespi: Welcome to the Science Podcast for May 1st, 2020. I'm Sarah Crespi. This is going to be our first Coronavirus-free episode in a while. First up this week, I talk with staff writer Jocelyn Kaiser about a study involving 10,000 women who all received a blood test for multiple types of cancer. Are blood-based biopsies coming to a clinic near you? Then we have researcher Timo Reinhold. He's here to talk about his paper on how the Sun is a lot less variable in its magnetic activity compared to similar stars. What does it mean that our sun is a little bit boring?

00:47 SC: Now, we have staff writer Jocelyn Kaiser. She wrote a story this week about a large trial of a blood-based test for different kinds of cancer. Hi, Jocelyn.

00:56 Jocelyn Kaiser: Hi.

00:57 SC: Who is producing this test and who's testing it?

01:00 JK: The test has been developed by a group of researchers at Johns Hopkins University, and they have been working on the test for years, they call it CancerSEEK. And last year, the company picked up the test, it's called Drive.

01:11 SC: What kinds of cancer can be detected with a test like this?

01:15 JK: In principle, many different kinds of cancer, and in this test, the cancers included liver cancer, ovarian, breast cancer, lung cancer, thyroid, lymphoma, and some other types.

01:27 SC: What were they detecting in the blood that could catch all these different things?

01:31 JK: So what they were detecting was DNA that is shed by cancer cells when they die into the blood, there are tiny amounts of it, but it is a signature of the cancer because certain genes are often mutated in cancer, that's what drives the cancer's growth, and so, by looking for 16 different genes, mutations in these genes, in the DNA, in the blood, the researchers could detect various types of cancer.

01:58 SC: But they didn't necessarily know what kind of cancer it was by looking at the result of the blood test?

02:04 JK: They didn't necessarily know the type of cancer or where it was in the body.

02:08 SC: Let's go to the study here. So can you talk about the group that participated in the study?

02:13 JK: Sure, but just to tell you what's different about this is until now, people developing these tests have been developing them by getting a big group of people, some of them with cancer that know that they have cancer, and the other group of people don't have cancer and they've looked at whether their test can tell who has cancer and who doesn't. What's different here is that they took another big group of people, women in this case, and what they want to know is, we don't know if any of these women have cancer or not, we think they don't have cancer, but we know that some of them probably do, and that is the more real-world situation where you'd be using a test like this. So that's what's so important. And they recruited about 10,000 women who all get healthcare in Pennsylvania through the Geisinger Health Care System, and that's the group that took the blood test.

03:00 SC: How long did the study go on for?

03:02 JK: I think it's been going on for at least a couple of years but each woman, when she enrolled in the study and got her blood test, she was then followed for a year.

03:11 SC: What happened if a woman in this study had a positive result on her blood test?

03:16 JK: If she had a positive result on the first blood test, she was asked to come back later for a second blood test that looked at a few more things in the blood to make sure that it wasn't a false positive, although it didn't rule out a false positive. And if that test was also positive, then she would be invited to come in for an imaging test.

03:38 SC: And the imaging would confirm the diagnosis?

03:42 JK: Yeah, so the imaging would tell her doctor if she did actually have some lump somewhere that might be cancer, but even then, you may have to do more. Well, usually you have to do a biopsy to make sure it actually is cancer because you can have lumps that aren't cancer.

03:57 SC: Overall, were they able to catch many cancers in this group of, what, 10,000 women?

04:02 JK: The blood test was able to detect 26 cancers in this group of 10,000 women, which doesn't sound like a lot, but there's actually not that many cancers that are going to pop up in a group this size, they found other cancers in other ways, but the total was only about 100 cancers.

04:18 SC: Now, what were they looking for with other methods and how did they compare?

04:22 JK: The other methods are what's called standard screening tests, like mammography, colonoscopy, and if you're a smoker, you might get a lung scan to look for lung cancer. Those are tests that are part of routine medical care, and part of the study's design was to keep encouraging women to do that testing because this isn't supposed to substitute for it. And those tests found another 24 lung, breast, or colon cancers.

04:47 SC: We have the blood tests start finding some cancers and the typical screenings finding some cancers. And overall, how many cancers did you say?

04:54 JK: There were another batch of cancers that were found through symptoms or other things that brought them to the attention of the doctor, so the total was 96 cancers.

05:05 SC: So is this a lot of cancer?

05:07 JK: The answer to that comes from epidemiology studies that look at how many cancers will occur in a group of women this age, which was 65 to 75, in one year, and according to that data you'd only expect about 100 cancers in one year in this group of women. That doesn't mean that this test found or this study found all the cancers, it may not have found all of them, but it is in the neighborhood of what you'd expect.

05:30 SC: One concern that a lot of people have about tests like this, screens like this is false positives, will something get flagged and it's incorrect, but then the patient has to undergo invasive procedures? Did that happen a lot in this study?

05:44 JK: In about 100 women, there was a positive blood test and the woman underwent imaging and she did not end up having cancer. In some cases, 22 cases, the way that doctors confirmed that she didn't have cancer involved an invasive test like a colonoscopy or in three cases, they actually did surgery. So there were women who had sort of a scare and had to undergo some kind of unpleasant testing, and in the end, they did not have cancer.

06:00 SC: What about false negatives? People who had cancer, but it wasn't detected by this blood test?

06:00 JK: False negatives would be the women whose cancer was found with conventional screening or symptoms and not by the blood test.

06:27 SC: And so the idea there is that, well, this will pick up more than the conventional approaches.

06:32 JK: That's right. The researchers say they're not saying they should for substitute for these other approaches. It should be additive to conventional screening.

06:40 SC: And that's something they tracked among the women in the study?

06:43 JK: Yeah. One question they had is if women were getting this blood test, would they think, "This blood test will find any cancer I might have. I don't need to go get my mammogram." But they encourage women to keep getting those mammograms. And they went back later, and they looked at their medical records, and found out that they continued to get mammograms, which is exactly what they hoped to see because they did not want to discourage them from getting those tests.

07:05 SC: One thing I found really encouraging from this study was... You mentioned in one draft of your story that I saw that a woman with ovarian cancer, that it was detected very early in her. And that is something that has proven really difficult to find before.

07:20 JK: This is a really good example of what the test's ultimate goal is. A woman who agreed to be on a video made by the Geisinger Health System and her name is Rosemary. And she talked about what happened to her, which is she signed up for the study, didn't think they were going to find anything, and then they told her she had a positive test. So she came in for the imaging, found out she had a stage one ovarian cancer, which is very small, the very earliest stages of cancer. She had surgery, and she says in the video that she hasn't had any side effects, and she looks really healthy, and she's getting ready to go for a walk with her husband. And that is really, ultimately, what this test is hoping to do. Because if it's caught that early and you have it taken out through surgery, chances are you're going to... The cancer is gone for good. Not always, but...

08:05 SC: What's next for this type of testing? More studies to kind of roll it out?

08:11 JK: Yeah. So that's a little unclear, because if you want to do things right and you want to go out and give this test to everybody and the researchers who develop this test can see it being given as a test once a year when you get your annual exam. Well, to get to that point, you have to do a lot more research. You have to look at whether it actually helps the people who take it live longer as a group than if they didn't take this test. Because, for example, it could be catching early tumors that would have been found before long anyway, so it's not worth the cost, or it could be finding tumors that were never going to grow. And so, that's not worth the cost either, and it may involve removing a tumor that didn't really need to be removed. The way you answer that question, how it affects the overall survival of the people taking it, is you do a very long study over many years, lots of people, where you have one group that gets the test and one group that doesn't. And you look at the end of the 10 years, or whatever it is, to see if more people are still alive from the group that took the test.

09:11 SC: That makes it seem like this isn't going to be rolled out any time soon to a clinic near you.

09:16 JK: Well, that could still happen because, for example, there's another company developing this kind of test named GRAIL and they are just starting a big prospective study like the one that was done by Hopkins in Pennsylvania. And they're talking about possibly commercializing their test in a year or so. So even though it hasn't gone through that sort of very rigorous long-term study that shows whether it increases survival, they could end up selling it and it might not be covered by your healthcare, you might have to pay for it yourself, but people could be asking their doctors to get it. And one person I talked to said the issue there is her patients come in with tests they've had done in that way that haven't really been validated, and they want her to do something about it. And the question is will doctors know what to do with this, will it be meaningful for the patient's care?

10:01 SC: All right. Thank you so much, Jocelyn.

10:03 JK: You're welcome, Sarah. Good to talk with you.

10:05 SC: Jocelyn Kaiser is a staff writer at Science. You can find a link to her story and the related research paper at sciencemag.org/podcast. Stay tuned for an interview with Timo Reinhold about comparing the sun's activity to other similar stars.

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10:24 SC: This week in Science, Timo Reinhold and colleagues write about how the sun is a lot less variable than similar stars. Timo's here to talk about how they figured this out and what it might mean. Hi, Timo.

10:35 Timo Reinhold: Hello.

10:36 SC: There are these records of the sun's activity going back a long time, hundreds of years. And even there's one case where we have a 9,000-year data set on changes in activity of the sun. Where do these values come from?

10:49 TR: The 100 years that you mentioned, so this is from 1600 something or 1500 something. So this is when the telescope was invented, and Galileo Galilei used it, for example, already to draw sunspots. So there exist drawings like several hundred years old from sunspots on the sun. And this is one evidence for magnetic activity. And then people started to take records of these sun spots. And yeah, since 1880 or so, we have really good coverage of these. So this is the magnetic activity, basically, the number of spots on the sun. This other time scale that you referred to, the 9,000 years, this is from cosmogenic isotopes. So this is from ice cores and tree rings which...

11:33 SC: Oh...

11:33 TR: Exactly.

11:34 SC: Why are you looking into this? What brought this question up?

11:36 TR: We are studying the sun and other sun-like stars in particular, and one way to compare the sun, to figure something out about the sun is to compare the sun with other stars which are like the sun, similar mass or temperature or radius and something like this. Therefore, we studied Kepler stars, which are similar in all the parameters that we could constrain, for example, effective temperature, especially also the rotation period of the star. We measured the variability of these stars, and found that there exist stars which are much more variable than the sun, although the stars are similar in all the other parameters.

12:14 SC: Right. And this has been something people had thought was going on for a while?

12:19 TR: Yes, exactly. The basic question is, is our sun quieter than other stars, or is it similar to other stars? And this is one question that we wanted to address and to answer.

12:25 SC: Right. How have people looked at this before, in other stars?

12:25 TR: On the one hand, you can measure photometric variability. So this is just observing the star for quite a long time. What we measure is the rotational variability of the sun. So on a rotational time scale, it's like a month or so.

12:25 SC: So the sun spins around once a month?

12:25 TR: Yeah, roughly. It's like 27 days. Yes, and then if you observe the sun for long enough then you can measure the variability of this light curve. We say light curves, so the brightness of the star varies. Yeah, because we have dark spots on the sun, and the sun rotates towards us, then becomes darker, and if it rotates... If the spots rotate away from us, so then it becomes brighter again. So you can more or less think of a sine wave if you want to.

13:14 SC: So, changes in activity are visible because dark spots show up sometimes. How does this darkening relate to activity?

13:21 TR: The origin of these dark spots is a magnetic field which emerges to the surface. The sun has a 11-year cycle, so every 11 years it's very active and then it becomes inactive and then becomes active again so it's like a very clear signal there. But we were studying the rotational variability on shorter time scales.

13:39 SC: In a calm time there'd be less difference as it rotated from one side to the other, but in the active side there'd be a lot more differences. You'd see a lot more variability in how bright the sun was.

13:51 TR: On the rotational time scales that's right, yeah.

13:54 SC: How did you collect information on other sun-like stars?

13:58 TR: We took data from the Kepler telescope and the Kepler telescope is a NASA mission which looked for planets around other stars. The good thing about this telescope is that it also monitored the brightness of 100,000 stars. Among these there are many solar-like stars. We studied the variability of almost 3000 stars in our final sample which are solar-like. Then we could determine the rotational variability on a four-year time base.

14:23 SC: When Kepler is looking for exoplanets, it's looking for changes in brightness in stars. So how is what you're doing different from that?

14:32 TR: If a planet orbits a star and then moves in your line of sight, so this is just a very short signal in time, it's just like a sudden drop in the brightness, whereas the rotational variability of the signal is a very different signal. A transit of a planet is much more periodic than the rotational variability, for example, so you can clearly distinguish these signals.

14:54 SC: Were the stars that you looked at for this study all rotating?

14:58 TR: For about 10% of the sample we had rotation periods measured for these stars. These are the stars which are interesting because we found that most of the stars where the rotation period could be determined, these stars are much more active than the sun. So whereas the other 90% where we don't know the rotation period because the signal is not periodic enough or they just don't have spots, the variability of these stars is much more like the sun.

15:23 SC: You found that when you were able to determine the period, how fast they're rotating, that they had a lot more variability in the four years that you looked at them.

15:33 TR: Yes, exactly. So, the stars where we know the rotation period they are a lot more variable, so they are on average five times more variable than those where we couldn't measure the rotation period, but there were also exist stars which are up to 10 times.

15:45 SC: If our sun has a big spot on it, how long does it take to appear and then disappear? Is it like a year? Is it like a month? I mean, how quick is this activity?

15:57 TR: This is the problem with the sun, because the sun spots have sometimes shorter lifetimes than one rotation period, so if a spot appears then it rotates away from you and if it doesn't come again because it died in the meantime, that's the problem.

16:10 SC: Yeah, I got it. So how did those data sets, humans' drawings of the sun over a couple hundred years, and this 9000-year data from ice cores and tree rings, how do those compare with what you found in your study? Do they match up?

16:25 TR: These recordings basically show you the 11-year solar cycle, and the solar cycle can be dated back these 9000 years or 600 or 400 years, and we showed in our study that this is also consistent if you take current data and measure the variability. So this nicely aligns with the magnetic activity. So you can really take the brightness variability as a proxy for magnetic activity.

16:50 SC: Could our son be in a lull? Could it actually have a period of extreme variability coming up sometime?

16:56 TR: This is one possible explanation of our results. We showed that there is a nice distribution of these variabilities. The stars where we could measure the rotation period, these basically populate the high variability edge, so it is possible that the sun once becomes much more active because we cannot distinguish the sun from all these other stars. Yeah, so this is one possible explanation, but time scale is hard to say. I mean, 9000 years the sun was more or less normal, as it is now, but 9000 years is nothing for a star. It's like a second for a human or so.

17:32 SC: Yeah. Thank you so much, Timo.

17:34 TR: Yeah, Sarah, thank you.

17:35 SC: Timo Reinhold is a post-doctoral researcher at the Max Planck Institute for Solar System Research. You can find a link to his paper at sciencemag.org/podcast.

17:46 SC: And that concludes this edition of the Science Podcast. If you have any comments or suggestions for the show, write to us at sciencepodcast@aaas.org. You can listen to the show on the Science website at sciencemag.org/podcast. There, you'll find links to the research and news discussed in the episode. And of course you can subscribe on Overcast, Stitcher, Spotify, Pandora, Apple Podcast, and many other places. This show was edited and produced by Sarah Crespi with production help from Podigy, Meagan Cantwell, and Joel Goldberg. Jeffrey Cook composed the music. On behalf of Science Magazine and its publisher, AAAS, thanks for joining us.