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Hello, I am Dr. Samjot Singh Dhillon and I am Chief of Pulmonary Medicine at Roswell Park Cancer Institute. Today we are going to talk about Pulmonary Nodules at a Glance.
I do not have any conflict of interest to disclose.

As lung cancer screening is becoming the standard of care, we are going to encounter more and more nodules on our low-dose CT scans. So the objective of this presentation is to enhance our knowledge about pulmonary nodules, to understand the different kinds of pulmonary nodules, to understand the concept of growth of pulmonary nodules, and to be able to look at some distinguishing features between benign and malignant nodules, and a brief overview of the different treatment management strategies for pulmonary nodules.

Basically, a pulmonary nodule is a small rounded or oval opacity in the lung which is less than 3 cm. If it is more than 3 cm it’s called a lung mass.

These CT scans show some different kinds of nodules. This is a less than 4 mm nodule which is usually benign. This is around 6 mm nodule in the left lung that needs to be watched more closely. And finally, the third CT scan shows a lung mass that is almost 4 cm in size.

In the National Lung Cancer Screening trial, even when they excluded all nodules that were smaller than 4 mm, they still found 24.2% positive screens or nodules. Now, 96% of these nodules were benign. So, it becomes very important to understand the difference between a benign nodule, or a nodule that needs to be watched, or a cancerous nodule that needs to be biopsied immediately. And it’s also important to understand which nodule not to biopsy and avoid unnecessary risks and complications.
To look at the base of the nodules, we used to see single solitary nodules, but with the advance in CT scan technology, now we encounter a lot of solitary nodules that are known as multiple nodules. In addition to that, we also see ground-glass opacity. The ground-glass opacities are increased areas of attenuation through which you can see the bronchi and vessels and the septae, and we are seeing them more and more. This could be due to inflammation; this could be due to fibrosis, premalignant lesions, but this could also be adenocarcinoma, and that’s why it’s important to follow them. Now, the ground-glass opacities could be purely ground-glass, just like this case, or they could have a solid component, and if there is a nodular or solid component in a ground-glass opacity, the risk of that being cancer increases from 18% to almost 64%.

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There could be a variety of causes for solitary pulmonary nodules or pulmonary nodules. The cancer is being the foremost, but infections like tuberculosis and fungi, inflammatory conditions like rheumatoid arthritis, sarcoidosis, arteriovenous malformations, and sometimes even mucus or intrapulmonary lymph nodes can also present as pulmonary nodules.

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When looking at pulmonary nodules, it’s important to look at the risk factors which help you to determine if a nodule is benign or malignant. Size is important; the larger the nodule, the higher the risk of it being cancer. Characteristics like a rounded margin, or irregular margin, presence of calcification, all these factors need to be kept in mind. Smoking history, which increases the risk of lung cancer, advanced age, presence of COPD, family history of lung cancer, and of course, asbestosis are other risk factors that need to be kept in mind when evaluating a nodule. If there are multiple risk factors present, then there is high likelihood that this nodule could be cancer.

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When evaluating a nodule, it’s important to understand the concept of growth. Typically we follow nodules for 2 years and if the lesions do not grow in 2 years, we call it benign. We also look at the diameter of a nodule, but it’s important to understand that it’s the volume that is growing, not only diameter that you seen on a single CT scan.
So, for example, in these images, we are looking at those nodules, these two nodules, and although it looks like that this nodule has grown significantly; both have just doubled in size, so they have same volume-doubling time which is the time it takes to double in volume. So, they’re growing with the same aggressive time; however, you may feel like that this one has grown faster. This is one of my cases where this small nodule took almost 2 years to grow where we could see the difference. And instead of biopsying it, we directly proceeded to surgical resection as there was no evidence of spread anywhere else. Now, if you try to do biopsy in this case and it’s positive, you’re going to take it out surgically if you can, and if the biopsy is negative the likelihood of this being cancer is so high, as this patient was a smoker, that you would have still taken it out. So biopsy would not really have helped in this situation, and therefore, we proceeded directly with surgical resection.

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It’s important to be able to distinguish some of the features that can help us decide whether this is favoring a benign process or a malignant nodule. For example: The size. Nodules less than 1 cm in size have higher likelihood of being benign and nodules bigger than 1 cm have a higher chance of being cancer. Then we have to look at the margins. Smooth and scalloped margins favor a benign process, while irregular or spiculated margins suggest a malignant process. Growth rate, or the volume-doubling time that I just talked about. If the volume doubling time is less than 20 days, that means the volume doubled in less than 20 days, it’s more suggestive of an inflammatory process than a cancerous process.

Similarly, if it takes almost 400 days to double that suggests a benign process or a slowly-growing cancer. Although ground-glass opacities are an exception and they generally do not follow this rule, but typically, 20 to 400 days is what it takes a malignant process to show a change in growth and that’s why we do CT scans over a 2-year period, and if you do not see a change in size, we presume most of these lesions are benign. Central, laminated, punctate, or popcorn calcification also suggests that this is a benign process; however, if you see speckled or eccentric calcification, it suggests malignancy. So, it’s important to look at the risk factors of the patients and the characteristics of a nodule to be able to make a decision whether you’re going to watch it, or you’re going to biopsy it, or you’re going to take it out.

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This is a case of ground-glass. You can see this small area of ground-glass opacity which is barely seen on a CT scan, and even when multiple CTs were done by the referring physicians, they could not see a significant change in size; however, when we separated out the CT scans over the years, we saw that this had grown slightly in 3 years. That is how a ground-glass opacity behaves. When we did surgical resection in this case, we actually found invasive carcinoma. Now, that's why it's important that the ground-glass opacities need much longer followup than a pulmonary nodule which is solid.

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In this case, actually these are 2 cases, where we saw calcification and presence of fat inside the lesion. These were hamartomas. These were not malignant lesions.

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So, along with all the other features, how do you work up a patient where you will see a pulmonary nodule? The first and the foremost thing is to try to get any old imaging. If you’re able to find old CT scans, old images, and it shows that the nodule has been present there for a while, that’s at 2 years, 3 years, then the chances of this being malignant are low and you do not have to put the patient or subject the patient for additional tests, biopsies, and imaging. For nodules that are bigger than 8 mm, we typically could order a PET scan to help us make a decision about a biopsy or surgical resection. If the nodules are smaller than 8 mm, typically the PET does not have very good resolution and you may not be helped by ordering a PET scan. Biopsy or surgical resection could be performed, based on the circumstances, and if the lesion is small or is favoring a benign process, and the chances of malignancy are on the lower side, you may decide to pursue CT surveillance. Now, when we do CT surveillance, it’s also important not to do too many CT scans and therefore adhere to the guidelines. In the past, we didn’t have any guidelines and we just watched these patients with CT scans, and multiple CT scans were done, but now we have guidelines which can help us to minimize the number of CT scans that are being done.

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These are the Fleischner Society Guidelines which came out in 2005. These are for pulmonary nodules that are solid. Basically, you divide the patient into low-risk category or high-risk category, the high-risk category being the smokers, family history, and asbestosis, and then you look at the size of the nodules. These guidelines are for nodules that are typically less than 8 mm. So if you have a less-
than-4-mm nodule in a low-risk candidate, there is no need to do additional CT scans. However, for high risk, you may end up doing another CT in 12 months and if the nodule is stable, no further followup is needed. For nodules that are between 4 to 6 mm, for low risk, another CT in a year will be appropriate, although for high risk you will do another CT in 6 to 12 months. If the nodule is showing any growth, you will biopsy it or remove it. Otherwise, one more CT in 2 years will be appropriate. Same is true for the nodules which are 6 to 8 mm or more than 8 mm. For example, a nodule that is bigger than 8 mm, you may do a CT in 3 months, or you can do a PET scan, or go for a biopsy. If you decide to go for a CT surveillance, you will do the next CT in 9 to 12 months and then another one in 24 months. So, basically, I’ll advise everyone to have these Fleischner Guidelines at hand if you decide to perform surveillance on these pulmonary nodules.

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As I said earlier, the ground-glass opacities are different. So the size of ground-glass opacity is important and the presence of a solid component, which increases the risk of lung cancer, is important. Now, we typically do a followup CT in 3 months in many of them because many times the ground-glass opacities could just be transient inflammation and it resolves; however, if it persists, then followup is needed. So let’s go back to this table and look at the Fleischner’s Guidelines for ground-glass opacities that came out in 2012. So, if you have a ground-glass opacity that’s less than 5 mm, a single opacity, no followup CT is needed. However, if it’s more than 5 mm, then you can do a CT scan in 3 months; if it’s persistent, then annual CT surveillance for 3 years. Remember, it’s not 2 years; it’s 3 years for ground-glass opacity. However, if you have a solitary ground-glass opacity with a nodular component, you can do another CT in 3 months and make sure it is not something transient. However, if it is persistent and less than 5 mm, you should follow them with a yearly CT for at least 3 years. However, if it’s persistent and if there’s a solid component, then biopsy or surgery will be appropriate. Now, these were the solitary ground-glass.

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We commonly encounter multiple ground-glass, multiple sub-solid nodules. Now, if these ground-glass opacities, if they are multiple and less than 5 mm, then CT at 2 and 4 years will be appropriate. If the ground-glass opacities are more than 5 mm and they’re pure ground-glass and there is no dominant lesions, then do a CT in 3 months, make sure it’s persistent, and if it is persistent, then annual CT scan for 3 years. Now, if in case, if there is a dominant nodule with part solid or solid component, then you should do a CT at 3 months. If persistent, biopsy or surgical resection, especially if the solid
component is more than 5 mm. You do not have to remember all of these recommendations but for all those people who are doing surveillance CT scans, I would recommend that you should have the Fleischner Guidelines for the solid nodules and the ground-glass opacities at hand, to know when to order CT scans, so you’re not following it up for short interval or too long interval, and you’re not ending up doing too many CT scans for the patient.

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So, in summary, pulmonary nodules are frequently seen on chest imaging. You’re going to see a lot more of them as lung cancer screening has become the standard of care. It’s important to look at the risk factors, size, and other characteristics of the nodules, so you can make an appropriate management plan for these patients.

Thank you very much for listening. I am Dr. Samjot Singh Dhillon. I am Chief of Pulmonary Medicine at Roswell Park Cancer Institute and if you have any further questions you can find us at: www.RoswellPark.org. Thank you.

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