And that's therapeutic de-escalation. How do we maintain cure and lower side effects? One of the major things that has been tried is minimising the radiation exposure. That can be done by avoiding radiation altogether or lowering the total dose, decreasing the field — now what that means is where the radiation hits in the body — and trying to avoid chemotherapy along with the radiation which increases the radiation’s effectiveness but also increases damage to normal tissues. There are strategies to identify who are the right patients, but right now that is limited to patients with small or early tumours based on T and N stage, so in other words how many lymph nodes are involved in the neck and how big is the tumour. And that's combined with minimal smoking history because we know that patients who smoke do less well after treatment. We've also used response to induction chemotherapy as a marker for who is gonna do well. If the tumour shrinks or goes away after induction chemotherapy we’d think we can use a lower dose of radiation. We’ve also done surgery and then worked on the surgical specimen, and if the pathological characteristics are favourable, we think we may be able to de-escalate. So let's talk a little bit about these different de-escalation strategies.

First, let's talk about radiation dose and field. And what you can see over on the right here is a treatment planning for radiation and the different curves are different radiation doses. And typically the highest dose is to the gross disease, or disease that you can see or feel. But lower doses go to other areas that surround this because we worry about spread of the tumour or lymph nodes in the neck. The primary tumour in the gross neck disease is a high dose, but the rest of the treatment area is gonna have moderate dose. And if you have more than a T2, or more than one lymph node in your neck, typically you get chemotherapy along with the radiation to make it work better; but it also increased damage to the normal surrounding structures. So, if we're talking about de-escalation of radiation dose and field, this might be a treatment plan, over on the left, and you can see the red area (and this is an axial slice, like we’re slicing across the jaw this way), the red area treats the gross disease, but you can see the yellow areas are treating both necks and that is still a significant dose of radiation. And there's some really important things in your necks, the choroidal arteries, the pharynx for swallowing, the tongue, and muscles in the neck as well, the bone also can be damaged with the radiation, and sometimes the bone will die after the radiation. So, the idea is to try to decrease the dose and what that means is we treat these normal fields but we just decrease, rather than giving a high dose in this area, we give a little bit lower dose, and rather than giving a moderate dose to theses areas, we give a little bit less of a dose with the idea that normal tissues may tolerate that better. We can decrease field. And what decrease field means is we may not treat any of these yellow areas, we may just treat the primary tumour or the gross disease in the neck and the primary tumour, or we may treat that plus one additional level in the neck; but not treat as wide an area. And by doing this we can decrease the side-effects from radiation therapy. But still, even with these de-escalation trials that have been ongoing, more than T2 or more than one lymph node requires addition of chemotherapy. I would say although these results are preliminary, and all these results are early, most of these studies have shown excellent survival and disease control at two years with faster recovery and decreased swallowing problems. So these have been very hopeful trials and they are creeping their way into more standard practice.