KAISORN CHAICHANA: But I'll be talking about a paradigm shift, extensive recession with deficit reduction and deep seated ICHs, or Intracranial Hemorrhages, and brain tumors. And so the problem with deep seated things that are located deep in the brain, you have to somehow get there without having collateral damage above those lesions.

Typically, everything in the brain goes from a diffuse area to concentrated area. So the deeper you go into the brain, the more concentrated the neural fibers are and the more important the fibers are. So anything that's deep seated is very high risk. In the past, it was very hard to access those regions. And I'll show you that.

So basically, whether you're doing a tumor or a blood clot or intracranial hemorrhage, the goal is minimally disruptive subcortical surgery. What that means is you minimally disrupt or minimally destroy. You don't want to have any collateral damage on your way to the lesion. Once you get to the lesion, you can remove the lesion without problems. The key is to get there without any problems.

So the subcortical space is a very vast space within the brain. And there's a lot of structures that go through that area. Typically, in the past, how people got to these areas, they used these bladed retractors. These bladed retractors that people place in the brain, they pull the brain to one side. Sometimes they use one retractor. Sometimes they used two. Sometimes they used four.

The problem with these retractors is anytime you stretch on those white matter tracks, you can sever those tracks. You can injure those tracks. And the deeper you have to go, the more damage you have. So that led the way to endoscopic surgery where you try to work through a very small tube where you have an endoscope going through that area.

But the problem with an endoscope is you can only limit your surgeries to fluid-filled cavities or air cavities where there's no blood. Anytime you have blood in that cavity, you erase your visualization. You can't do anything.

Retractions are a problem. We did this paper when we were at Hopkins with Dr. [INAUDIBLE] and myself. What we did is we looked at all the skull-based tumors that were operated on over a 10-year period. And we saw whether or not we used retractors on the brain.

What we found is if you use a retractor on the brain, no matter how long you use it, you cause collateral damage down the road. So when you got a scan six months or 12 months later, there'd be a significant amount of [INAUDIBLE] changes within the brain. So you want to try to avoid using retractors.

So how do you get to these deep seated lesions without using retractors? The way of getting down there are these tubular retractors and brain path is one of them. But there are also several different types. The real father of using these tubular retractors was Dr. Patrick Kelly out of Mayo Clinic in Rochester.

And so what he did is he designed these metal tubes that came in different sizes. They went from anywhere from 10 millimeters wide to about 3.5 centimeters wide. And what he would do is stick these tubes into the brain tumor and then resect them. And what he did is he did a mapping of each level below the cortical surface. And he drew a picture of that. So he knew if he was 8 millimeters below, this is how wide the tumor was. If he was 15 millimeters below, this is how wide the tumor was. And he'd resect those tumors.

The problem is he was very gifted in doing that. And when other people try to do that, they would have catastrophic results. And so this led the way to Amin Kasam and his design of this other tubular retractor that's clear instead of metal [INAUDIBLE]. And it was limited to 13 1/2 millimeters.

Reason why he limited to 13 1/2 millimeters is because in cadaveric studies, anything that stretches over 13 1/2 millimeters would sever the white matter tracts. So 13 1/2 millimeters is basically the diameter of a dime. So you want to work through a quarter of the size of a dime in order to minimize potential damage to those white matter tracts.

And why are the white matter tracks important? There are several different types of white matter tracts. In general, there's basically three types of white matter tracts. They're called projection tracts, association tracts, and commissural tracts.

Projection tracts are the most important. Those go from the brain to the spinal cord. And the most important one being the corticospinal tract. Association tracts are the fibers that connect the same lobes within the hemisphere. There are several ones of those that have different types of functions. And the commissural tracts are the ones that connect the two hemispheres, the corpus callosum being the most important of those.

So in the brain you have the cortex. Below that, you have the white matter tracts. And within the white matter tracts, you have projection fibers that go downwards towards the brain stem and the spinal cord. You have association tracts that connect the same hemisphere. And you have commissural tracts that connect contra-lateral hemispheres.

So the problem is when you're working through all this, you can't tell what is what. Some people do awake surgery to discern which tracts is what. But by the time you get there, you can have collateral damage. So the problem with all these previous clinical trials is that you have these deep seated lesions. You have to get there and you damage these white matter tracts on your way down there. And that's probably why a lot of the outcomes were not very good.

So for intracerebral hemorrhage-- Dr. Freeman touched on this-- it's a major problem. In the United States, there are about 800,000 strokes per year. Of those, intracranial hemorrhages only account for 10% of them where 87% are ischemic.

However with these intracranial hemorrhages, hypertension is the leading cause of that. The early mortality is up to 30% to 50%. Of those patients that have survived with an intracranial hemorrhage, 80% are left with significant deficits. And only 12% to 39% return to independent function. So even though it only accounts for about 10% of the strokes, economically it counts for $12.7 out of $74 billion direct costs for stroke as compared to the other causes of stroke.

So as Dr. Freeman touched on, the standard of care is basically blood pressure control even though there's not a lot of studies showing that. As you can see, the level of evidence is very low. You want to optimize CPP and lower ICPs. You want to reverse the coagulopathy. And if there's intraventricular hemorrhage, you have CSF drainage. And there's other supportive care in multi-system hemeostasis.

So basically, surgery right now is not advocated for these lesions unless it's a cerebellar hemisphere that is greater than 3 centimeters in size. The only time it's really advocated for cranial is that a cranial surgery is if it's life saving. So if someone comes in and they're herniated or it's a lifesaving procedure, then you can evacuate the clot. But right now, this is what the trial's designed for, to see if it's efficacious to evacuate these clots.

And so here's a meta-analysis of those previous surgical trials for intracranial hemorrhages. And you can see, these are the four meta-analysis. And they basically have all insufficient evidence to have a conclusion. The STICH trial, which Dr. Freeman alluded to, so the STICH one, what they did is they compared early surgery versus initial conservative management in patients with spontaneous intracerebral hematomas.

So it was 1,000 patients from 83 centers from 27 countries that were randomized either into surgery or conservative management. The conservative management was the blood pressure control, CPP optimization, and so forth. And what they found was that favorable outcomes for early surgery was 26% versus initial conservative treatment was 24% but was not significantly different.

When they looked at lobar hematomas without intraventricular hemorrhages, what they found was that the favorable outcome was 49% in those with early surgery versus 37% and it trended towards significance with a p-value of 0.08. What they concluded, though, was that STICH lacked sufficient power to address this subgroup.

And so that led to STICH two, where they did the same study but just those with lobar hemorrhages without IVH. So they compared craniotomy versus best medical therapy for lobar spontaneous ICHs between 10 and 100 CCs with no associated intraventricular hemorrhages. Same as STICH one, 78 centers in 27 different countries. 600 patients were enrolled.

And what they found was there's not really a significant difference between the two. But there's significant overlap or 20% crossover from the conservative management to the surgical arm. And the difference was 3.7% in favor of surgery, but it wasn't statistically significant. So the conclusion from these studies was that surgery was not efficacious for intracranial hemorrhages in the [INAUDIBLE] space.

But the problem is when they did these surgeries, the way you evacuated a clot or you treated a clot was very different among the 27 different countries. So some people would just do a hemi-craniectomy, which means they removed the bone to help the intracranial pressure. Some would do a large craniotomy and evacuate the clot. Some others would just evacuate the clot through minimally invasive means.

So this led to MISTIE two, where they study minimally invasive surgery for intracerebral hemorrhage evacuation to determine if minimally invasive procedures were efficacious. This was not a study designed to evaluate whether it's better than conservative management. It's mainly a safety trial.

And what they found when they compared those with medical versus surgery, though, there is a 14% difference in those that underwent surgery in terms of regaining independent function which is based on a modified Rankin score between 0 and 3. When they looked at the costs, what they found is there's a 38-day length of stay reduction among the surgical arm and there is a $44,000 savings per patient in the surgical arm.

When they looked more closely at the clot volumes, what they found is that the less clot you had in the brain, the better your outcomes were. So if you had less than 10 CCs of clot, your chance of having a meaningful recovery or modified Rankin score between 0 and 3 was 60%. If you had greater than 35 CCs of clot, then your chance of an independent recovery was less than 10%. So this led to MISTIE three. And once again, Dr. Freeman alluded the results aren't up yet, but hopefully soon.

But these previous trials basically show there is a benefit of MIS approaches over other approaches. There's a benefit of surgery over conservative treatment in certain subgroups. There's a benefit for early surgery, which means you evacuate the clot early rather than letting the clot sit there. And there's a positive impact on functional outcomes, there's increased acute care cost savings, and reduced length of hospital stay.

The challenges of these, though, is that what is early clot evacuation. So requirement of clot stability from these [INAUDIBLE] MISTIE is that in order for you to qualify for MISTIE, the clot has to be stable for 6 to 12 hours. So any clot that's expanding, it automatically disqualifies them from the MISTIE trial.

So as you know, most of these clots are expanding. And I'll have slides of that. So a lot of patients are excluded from getting any type of therapy. It's also difficult to address active bleeding. So if you have a spot sign when you get a CTA, which means there's active extravasation of blood, these patients don't qualify for the MISTIE trial as well.

Also, whenever you have a primary bleeding, there's always a risk of further bleeding down the road. And then clinical trials for surgical ICH evacuation, though, have not consistently shown improved patient outcomes. But the surgery arm is very diverse. So common factors that need to be considered in these approaches for a study is the timing of intervention, when that therapeutic window is, the technique that is used, the patients that are selected, the technology that is used, and the training and education involved.

So the rationale for early intervention for clot evacuation is that 30% to 40% of the hematoma for patients that present with intracranial hemorrhages expand. So a third of them gain from their initial volume where they increased by 33%. A lot of them have a spot sign, which means active extravasation. If you're able to evacuate the clot, you can have rapid correction correction of intracranial hypertension. And if you can reduce the length of stay, you can improve medical complications which are pneumonia, aspiration, respiratory failure, PE, and sepsis, among others.

So here's a classic example of a medical management of a clot. A clot comes in. They have intracranial hemorrhage and that clot sits there. As these blood products break down, it releases a lot of pro-inflammatory markers. So calcium gets an influx into the cells. It damages the mitochondria and causes cytotoxic edema necrosis.

All these cells, including red blood cells, hemoglobin, plasma, proteins, and others are breaking down and causing microglia activation. It's pro-inflammatory, leads to blood-brain disruption. So a lot of damage is sitting there while the clot is sitting there. So the goal of this enriched trial is to see if early evacuation of these clots results in improved outcomes.

So the study purpose is to determine if minimally invasive parafasicular surgery using current available and FDA cleared technology for early intracerebral hemorrhage evacuation results in improved functional outcome and economic benefits when compared to standard medical management. So we just had the site visit yesterday. So we should be up and running shortly.

And inclusion criteria for this is anyone between the ages of 18 and 80, CT showing acute spontaneous primary ICHs so not ICHs from AVMs or other causes, a GCS between 5 and 14, an ICH volume between 30 and 80 CCs. And the study intervention would be within 24 hours of the last known well with the goal of being less than eight hours. And they have to also have a historical modified Rankin score of 0 to 1, which means that they're independently functioning.

So here's an example of an intracranial hemorrhage case. So here you see a left-dominant hemisphere basal ganglia hemorrhage and the after procedure's below. The DTI images are shown below that. And you can see, the internal caps and all the tracts were displaced immediately so we can come from an anterior approach through the trans-sulcal approach. And as you can see, we can do a small opening in the dura which is only about 15 millimeters. And here's the clot evacuation.

So we target the sulcus. The sulcus is the area between the gyri. And by targeting the sulcus, you preserve the projection fibers and the association fibers because those are not usually within the sulcus. Instead, you engage the U fibers.

And so usually overlying the sulcus is a vessel. And you can see here, there is a large vein. And so with the brain path device, it has a pointed probe that allows everything to be displaced including the white matter tracts rather than severing them. So we place the brain path retractor and it's also vented. And because there's increased intracranial pressure from the tumor, it gets vented out the shaft of the retractor.

And here we're passing the device in. And as you can see, the clot comes out. And then we can easily recognize what's clot and what's not clot. And then after, we remove the retractor and the vessel's preserved.

And so similar to that, my specialty is mainly brain tumors. And we can also do that for brain tumor resections. So here's a study that we did out of Hawkins that show in order to make a meaningful difference for patients with deep-seated tumors, you have to have 70% resection or less than 5 CCs of residual volume.

And so what we found, though, is that if you have 70% resection, you improve the survival from 8.8 months of 14.3 months. And you decrease the delay in recurrence from 6.4 months to nine months. And then with residual volume, if you're able to decrease it less than 5 CCs, then you increase the survival from 11 months to 14.9 months and you delay the recurrence from 7.4 months to 8.9 months.

The same is true for older patients. If you try to operate on older patients, the more you resect, the better their outcomes. And here's a survival [INAUDIBLE] for older patients where survival goes from four months to 6.7 months. And even for poorly functioning patients, you can improve their outcomes by resecting more tumor.

However, this is all with the caveat that if you cause a deficit, you reverse any benefit you have for extensive resection. And so that's where the clot comes into play. So if you're evacuating an ICH and you cause iatrogenic damage from that ICH, any clot you remove, you negate the benefits of that.

And so here's another video. These are deep seated tumors that we did. Here's four different cases. And we published this result.

So here's an example. Here's a 63-year-old male with right-sided weakness and speech problems. His motor strength was two out of five, and improved to five out of five post-operatively. Gross total resection pathology is a GBM. He was recurrence at nine months. Avastin was added, and his overall survival-- he was alive at 12 months.

Here's a younger patient with a left thalamic tumor, dominant hemisphere that we used the brain path approach. Similar outcomes. Here's a video of that. So once again, we're targeting the sulcus. The other thing I should mention is that typically to look down these tubes, we use an exoscope, which is like an endoscope but it hovers over the surgical field. And we're looking at a 2D screen here opening the sulcus.

And so we're parting the natural corridors in the brain to use those natural corridors to try to minimize any collateral damage. And so here we pass the brain path device. And now we're resecting the tumor by having a protected channel so there's no collateral damage on the side. You can see there's a little bit of bleeding, but allows us to pinpoint where it's bleeding. And then after, everything comes back together as though we weren't there.

These are other examples of deep-seated tumors. This is a left basal ganglia and a right [INAUDIBLE] lesion. Some inclusion, frequency of ICHs in GBM high-grade gliomas are increasing. Outcomes tied to extent of resection and avoidance of deficits. Morbidity is associated with access and can be minimized with minimally invasive techniques. And extensive removal can be achieved in deep-seated locations with the use of these retractors. So thank you.