I am dimitra's mistress I am with a Brigham and Women's Hospital and Harvard Medical School and I will be talking today about the hemodynamic(血流动力学) significance of stenosis from CT angiography specifically from the transluminal attenuation gradient perspective(我今天要谈的是CT血管造影对血管狭窄的血流动力学意义，具体来说，就是要从平移衰减梯度的角度谈。) so if you think about lesion(病变) significance, the end result of it is a lack of oxygen supply to the underlying myocardium and CT perfusion can show us that similarly CT the CT angiogram can show us the conduit very well and but in between the two between the conduit where the blood flows and where it goes and whether it reaches there there is the blood flow and CT currently does not have the ability to show us that at all there are a couple of solutions that are starting to emerge one of them is the now-infamous heart flow technology which is based on computational fluid dynamics and then there's another camp which is the transluminal attenuation gradient(腔内衰减梯度) which is based on looking at the contrast kinetics within the CTA and I will also talk a little bit today about the what I think might be the future convergence of the two technologies so let's start first with what is the tag and some results to date and some case examples so the tag emerged from the observation then when you that when we got the first 320 detector Oct we expected a coronary artery which is imaged at the in its entirety in a single moment in time to have the same opposite occation throughout its length however what we found is that even in normal arteries there was a small drop off in enhancement from approximately two distally about 45 Hounsfield units the same among all the main coronary arteries when we looked at coronary arteries with significant stenosis actually there's a mistake it should be greater than 75% lesions that drop-off was much larger so that gave us the impression that there might be something in the contrast enhancement along a vessel at ISO temporal 320 detector Oct that might convey something about the so the tag basically was a easy way to summarize that drop-off in contrast enhancement along the artery if you think about the proximal luminal enhancement measurement and the distal luminal enhancement measurement basically you can put them in the houseful you can take the Hounsfield units put them in the graph where the x-axis is just the distance between the two locations of course instead of doing this at only two locations you can do it at very regular intervals along the length of an artery and make a very dense graph which you can then summarize with a simple linear regression and come up with a number that tells you what is the average drop off in enhancement a per centimeter of artery in this example say minus 8.3 Hounsfield units per centimeter order meaning that if the proximal value is 300 hands-full units and you go ten centimeters further down the artery you expect to find about 217 hounds four units in the lumen now one of the nice things about the tag is that because it is a linear fit over very dense data set it is easy to compute but it's also very robust in the presence of artifacts such as say for example beam hardening due to calcium or errors in your segmentation now a number of groups have looked into validating the use of tag with respect to detecting functionally significant stenosis and those are typically described by the fractional flow reserve and one of the studies from the Melbourne the Melbourne group here shows that tagged computed from 322 tetra Rossi team significantly improved both sensitivity and specificity to detect a clinically relevant reduction in fractional flow reserve if you take a closer look lo though at the scatter plot you will see that the correlation between invasive FFR and the transluminal attenuation gradient while it is there is not exactly strong and this is something that I will come back to again later on now in terms of the other studies that have been done they all have shown a correlation between tagging fractional flow reserve but similar scatter plots in fact to date only 320 detector Oct seems to provide a tag value that actually correlates with fractional flow reserve 64 and lower detector rows and even 256 one study more readers recent than as shown here did not find a significant reclassification of patients now some examples here up on the left side there is a case with a spec defect in the led territory and a large tag of minus thirteen point three huntsville units per centimeter and on the right there a normal coronary artery by CT a with a much smaller tag of minus four point six Hounsfield units per centimeter as you would expect here is another example with a case with a fractional flow at lesion with a fractional flow reserve of point 33 very significant and a similarly large tag of minus fourteen point six Hounsfield units per centimeter but now here on the right there is another case that is normal by CTA and it has a tag that is much larger - twenty three twenty point three Hounsfield units per centimeter so one might ask first why is this happening and secondly how are we gonna deal with it let me put that aside for a little while and let's go back to lesion hemodynamic significance and look at fractional flow reserve and other ways for CT to give us that information about the hemodynamic significance of a lesion in a invasive catheterization one is looks at the pressure proximal and distal to a stenosis and if their ratio is less than 0.8 then the lesion is thought to be hemodynamically significant in the sense that it's actually impeding flow it's causing resistance to flow in a normal car deal artery there should be no pressure drop needed to drive the flow course it's been shown that FFR is currently the best way to determine whether a lesion should be intervened upon or not and this is a result from the large fame study that showed that event freezer I've always bad better when PC I was guided by FFR rather than an Geographic means which just looks at the percent stenosis now FF RCT is a new technologies the first of the two solutions that are available for the four using CT to get to human dynamic significance of a lesion and basically what it does it starts with your CT and gives you a simulated FF R value now how does it get to that value well the way you start is by segmenting the coronary human from your CTA and this segmentation produces a computer model a mesh that a computer can use in conjunction with a set of values that you give it describing how much flow is going into that model and how much is coming out of each branch given that information a computer can solve the equations of motions for the fluid flow and come up with a nice solution which then can be translated into pressures and from those pressures you basically can have a simulated FF R value of course depending on the conditions that you give the computer and ask it to solve them the system of equations it'll give you a different set of pressures and therefore a different FFR for example in this lesion here one simulation might produce an FF R of 0.89 which is not significant and another one might produce an FF R of 0.68 which is significant considering the pointed cutoff used clinically so which one is correct and why do they do we get the two different numbers well these two simulations were done as follows one if they both assumed a hyperemic flow out of 439 million liters per minute but the first one assumed that the LA D territory only requires 86 milliliters per minute whereas the other one assumed that the lady territory required 345 milliliters per minute and those two solutions basically gave us the different FFR now Hart flow had compare it's a company that has one way of picking those value and coming up with a good solution to the FFR problem and they do this with a very complicated system of equations that considers the entire circulation in the human body as a very simplistic but very accurate model of an electrical circuit and then coupling that with the three dimensional CFD of the coronary arteries unfortunately this coupled system of equations does require a supercomputer some say to solve it does require quite a lot of computational power and that has been one of the main critiques of hard flows of FRC team now on the other hand the results of that afar CT have been quite good to date there have been three large clinical trials all of them showed a very good correlation between ffs are computed from CT and invasive ffs are all of them have shown an ROC curve area under the curve of about 0.9 and higher this is a technology that I believe in works very well and it'll definitely be used in the future however if you do take a closer look at the data and you look again at scatter plots just like we did for tag you will see that even though the correlation is there and it's very good and it does allow us to reclassify a lesion as being significant or not the correlation is also not as tight as we'd like so putting the two together FF RCT versus invasive FFR and another example of tag versus invasive FF are we see that the correlation is the plots are pretty much not that different so tag does carry information about hemodynamics but it seems that we're not getting at it correctly and this is the next step I think which is we need to understand what tag really means and then we can figure out how to correctly use it to quantify lesion hemodynamic significance and towards this this end let's take a look at you know a standard CT as it would happen you inject the patient with a contrast agent the contrast agent starts to flow through the vasculature either in the proximal location here the ascending aorta and then it goes out through the descending aorta and we have those two contrast passage curves now your volume CTA or spiral CT or whatever it is is acquired at a certain time when you think that you have enough contrast in the arteries to get a very nice image but let's take a closer look at this problem so let's say that someone gave you those two contrast passage curves in two locations in the vasculature the proximal location and the distal location what is the first thing that you would do first thing that I would do is I would calculate the time between the two curves why well because this time delta T is the time that it took contrast to flow from proximal location to distal location what's the second thing that you would do second thing that I would do is I would calculate the distance between the two locations that those curves were acquired at why would I do those two things well because that's just velocity Delta X divided by delta T and of course we have love blood velocity you can get blood flow volumetric blood flow as area times velocity cross sectional area of the vessel times velocity now the limitation of CT in a way for trying to get this type of flow information is that you only get information from a single moment in time with a volume CT now in that CT all you have really are of course the distance still and the only thing that you can see regarding the enhancement is the proximal and distal enhancement so how do we translate this information that tag effectively uses into flow well let's look at this difference in Hounsfield units a little more carefully let's make the assumption that at the moment at around the time that the CT a was being inquired contrast was rising at a fixed rate let's say 35 Hounsfield units per second and now let's say that the distal location is 70 Hounsfield units less than the proximal location how long will it take if enhancement is rising at 35 hounds will per second for the distal location to rise by 70 Hounsfield units um of course it's gonna take just two seconds now if I tell you also that the distance between the two points is 16 centimeters then what is the blood velocity 16 divided by 2 8 centimeters per second now if you work through the mathematics of this basically what we have done is we have related the difference in Hounsfield units at two different locations in the vasculature with the rate of contrast increase in time add around the time that the CT was acquired times the time difference the delay in time that it takes for contrast to go from one location to the next and tag is nothing more than this difference in housefull units expressed as a per unit distance of vessel if you work further through it you find that there's a very simple relation relating the velocity and the inverse of the transluminal attenuation gradient so blood flow is in fact nothing more than something that has to do with the inverse of tag times some parameter alpha that encapsulate among other things the rate of contrast increase during the CT acquisition and the vessel cross-section now let's look at a very simple example here on the left there is the bolus tracking ROI values Hounsfield units as you're waiting to start your CT acquisition and you fit that to see that you have about a 50 5.6 Hounsfield units per second increase in contrast enhancement then you trigger your scan the bolus tracking ends and a couple seconds later you acquire your CTA let's go to the CTA and measure the tag and we get the tag for the RCA and we will find that using this information that flow the volumetric flow through this RCA comes out to be about a number of 55.3 we do the same thing for the alady 105 points lcx 123 point 3 now those numbers look suspiciously like the actual volumetric flow rates that you'd expect in a left dominant circulation which this is the CTA is an example of so and in fact this is precisely what we did for a first level validation of this underlying physical principle and what we did is we looked at precisely right and left dominant circulation where we know from large trials what the average flow going in down inch main coronary artery is we then took a small number of CTS and looked at what relative flows they give using this information and what we found is that in fact we get fairly relevant numbers that follow the expected patterns of relative flows now that we have an idea towards what tag really means the next question to ask is how can it be used to determine lesion significance correctly well there are a number of factors that go into this model and we need to make sure that each one does in fact correspond to what we do in practice so for example if we take tag and correlate it directly to FFR we need to ask well how about the rate of contrast to increase leading up to the CTA is that can that be dropped so that we don't have to account for it and do this correlation secondly we need to ask well when does the tag in fact reflect flow when does this model hold and thirdly we know that the lesion significance is defined at stress not addressed and CTA is performed at rest so any information that we can extract from CTA regarding blood flow will be about rest flow regarding the first item on the list well we know a number of factors that affect the contrast passage after an intravenous injection and some of them actually do change the bullish the bolus shape so that in fact they do change this assumption this assumed alpha factor does change based on a number of both patient-specific as well as scan parameters such as injection rate or what protocol you're using and blood volume so it appears at least at first the tag cannot be directly compared between patients as for the second item on the list when does this model hold well it appears that it the the intrinsic assumption is that the moments leading up to the CT a contrast in flow increase was was fairly constant this only holds during the up slope of the contrast passage and also in the down slope but this does not hold during the up slope so you need to perform your CT a at the right time in order to be able to extract information about flow using tag as for the last item how can we use tag correctly to determine lesion hemodynamic significance as defined by FF our well if we can inform the boundary conditions for the computational model using the transluminal attenuation gradient and its relationship to flow to determine how much flow is going down each branch of the coronary artery tree then we can scale that to hyperemic flow and end up with a FFR that is simulated but from patient specific flow conditions that were measured directly from the CT a so in in summary what we can fairly confidently say is that coronary contrast enhancement and it's drop-off along a vessel as determined for example by the tag under certain conditions is a compendium of factors with flow being just one of them these factors are however very specific in and can likely be explicitly calculated from the CTA so that would mean that we can get rest flow from CT angiography using something like the tag and that also however means that the flow that we get because its rest slow it probably doesn't as directly correlate to FFR as we would like and one way to overcome this last final problem is to use the information that we obtained for flow from the CT angiogram as patient-specific boundary conditions to calculate FFR thank you