Dr. John Colberg and Dr. Richard Peschel, Surgical and Radiation Treatment for Prostate Cancer December 7, 2008Welcome to Yale Cancer Center Answers with Dr. Ed Chu and Dr. Ken Miller. I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and an internationally recognized expert on colorectal cancer. Dr. Miller is the Director of the Connecticut Challenge Survivorship Program and he is also the author of "Choices in Breast Cancer Treatment." If you would like to join the discussion, you can contact the doctors directly at canceranswers@yale.edu or1-888-234-4YCC. This evening, Ed and Ken welcome Dr. Richard Peschel and Dr. John Colberg. Dr. Peschel is Professor of Therapeutic Radiology and Dr. Colberg is Associate Professor of Surgery, both at Yale School of Medicine.Chu John, let's go ahead and start off by defining the population of males who are at an increased risk for developing prostate cancer?Colberg Any man over the age of 50 is considered at risk for prostate cancer. There are some specific risk factors though. You can look for family history, meaning one or more first-degree relatives, father, brothers, or uncles, that had prostate cancer, and you can also look at race. We know that African-American men have a higher incidence of prostate cancer and have more risk of disease at diagnosis. And finally age, the older you become, the greater risk you will have of getting prostate cancer.Chu Unfortunately, for all of us males, there is always the risk for developing benign prostate diseases. If a male were to develop a benign prostate disease disorder, does that place that individual at increased risk for developing prostate cancer?Peschel No, it does not appear that way. The problem is that it develops in the same group of men, the same men who develop a benign enlargement, or BPH, also are at risk of developing prostate cancer, but benign disease does not confer an increased risk of prostate cancer.Miller I have heard a wide variety of estimates so maybe we can clarify, but if we live long enough, if a man lives to age 70, 80, or 90, what is the chance that there is some cancer in the prostate, or a cancer that will cause him trouble?Colberg Well, those are certainly two different questions. If you look at autopsy specimens, which we base that on, you can have prostate cancer as young as age 30. Men who are in their 80s and 90s, probably 70%, maybe 80%, of men will have a small focus of prostate cancer. It is probably not significant and there are lots of different definitions of insignificant prostate cancers, volume, Gleason grades and scores, etc., but yes, the older you become the greater chance you will have prostate cancer. That number, if you live long enough, may be up to 100%.Chu I am just curious, if prostate cancer were to hit someone at the age of 30 or 35,3:01 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Dec-07-08.mp3 would you automatically assume that cancer is going to be more aggressive than say if it were to affect someone who is 75 or 80 years of age?Colberg I think that the younger you are the more concerning it is, not to say that people in their 70s do not get aggressive cancer because they do, but certainly you have a lot more years to live when you are 35 or 40. Again, it is pretty uncommon. I will see a handful of men a year in their 40s that have prostate cancer. It is not a real common entity because we do not for it. We do not

draw PSAs or blood samples routinely in men in their 30s and 40s unless we have a specific reason.Peschel I think the key to answering your question is that we do have a marker for aggressiveness and that is the Gleason score; what does the cancer look like under the microscope? So, independent of age, you have a pretty good estimate of how aggressive the cancer is going to be based on the Gleason score.Miller In terms of screening, what are your recommendations and your thoughts in terms of what is good screening and at what age?Colberg For the average American male, screening should begin at about 50 and should include a PSA, a rectal examination, and should occur once a year. There are subgroups of patients that should be screened earlier, such as patients with a strong family history, or African American males for instance, probably should be screened earlier.Chu What PSA number does one need to begin to worry about? A lot of my male friends, who go to the doctor and get the PSA, are really obsessed with the number that comes back. What does each of you tend to think about in terms of the number that one needs to be worried about?Colberg Historically, the number has always been less than 4, and that is probably not appropriate, especially the younger you are. There is what is called age reference PSA levels that one looks at, but more importantly, it is what happens to the number over time. For example, if you come in and your PSA is 2, certainly that is within the normal range, but it is more important what happens over time. If that number jumps up to 3 or 4 over a year's period of time, even though it may be normal, that is kind of a red flag that something probably should be investigated. It is a little bit of a gray area for us about what actually is a normal PSA level, but certainly under 4. The younger you are, the lower the number is, so if I see a man who is 45 in my office and his PSA is 3.5, that is probably too high. But if I see an 80-year old man or a 75-year old man in my office and his PSA is 4.1, that is probably okay.Peschel The other thing we are learning, particularly with the epidemic of obesity in this5:47 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Dec-07-08.mp3 country, is that the PSA has to be corrected for weight. Obese men have artificially low PSAs and you have to make some adjustment for that.Miller I have to say, that is a new bit of data.Peschel It is very interesting and discouraging to be honest with you, because of the outbreak of obesity that is coming.Miller Let us get back to this issue of genetics and heredity, or the inherited risk. Do we have any idea why, or what the mechanism is? Is there a gene that we have identified?Peschel I do not think we know the cause of prostate cancer. Certainly, there seems to be environmental factors that are very important. There are some identified genes in the African-American population for instance, but 10% of African Americans have an identifiable genetic mutation that puts them at risk for higher and more advanced prostate cancer. In our department, we are studying a nick in the DNA that can be identified and associated with prostate cancer and higher failure rates. We are looking, but we have not found a full answer yet.Colberg And I think most prostate cancers are sporadic just like colon cancer, breast cancer, or kidney cancer. There is a genetic component in a small portion, but most of them are sporadic, they have no family history or family history that is

significant.Miller What are some of the typical symptoms that an individual might experience?Colberg Most patients do not have any symptoms. The main reason they come to the office and have been biopsied or diagnosed with the prostate cancer, is because they have had an elevated PSA level. Occasionally, they will have some BPH symptoms described earlier, slowing of the stream and getting up at night, but those are not specific for prostate cancer. It is pretty uncommon now-a-days to see people who come in with symptoms of metastatic disease, or advanced disease like bone pain, pelvic pain or urinary retention, things like that, which you used to see 20 or 30 or 40 years ago. You do not see that very often. Most men have no symptoms with their low grade or localized prostate cancer, early prostate cancer.Peschel I agree with that. Most men have symptoms because they have benign prostatic hypertrophy, and that is what brings them to the urologist. Almost nobody has a symptom anymore from prostate cancer because of PSA screening.Miller When we talk about cancer in general, people are scared. I think this is one of8:23 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Dec-07-08.mp3 the reasons why men and women do not do the tests that perhaps they should have done, but if you are suspicious as a clinician that someone may have prostate cancer, how do you make the diagnosis? Is that a big operation? Is that something for people to fear and avoid?Colberg People will usually come in with an elevated PSA level, or during an examination with your finger, when you feel the man's prostate if there is a lump or a nodule, or firmness, and the way we make the diagnosis is with a biopsy done in the office. They are called transrectal, meaning we put an ultrasound probe in the rectum and we take the biopsies of the rectal wall under local anesthesia, and it is an office procedure. It is very well tolerated. It is not painless, it is uncomfortable, but it is well tolerated and usually we will have the answer in 48 to 72 hours when the pathologist looks at the slides.Chu Then once the diagnosis of prostate cancer is made, what goes into the decision making process as to what treatments should be recommended to that individual?Peschel There is a wide spectrum of choices that patients face. You look at their general health, commorbidities, their age, their Gleason scores are particularly important, the PSA which is the blood test, and then their physical exam. The choices that you can lay before them go all the way from careful observation without treatment, surgery and radiation therapy, so it's a wide choice, but it is all based on general health, PSA, Gleason score, and age.Colberg There is no one cookbook answer for every patient. I try to emphasize that with my patients, that a decision that is right for them, may not may be the same for someone else. Someone may be a very good candidate for surgery, and another person may be a better candidate for radiation therapy. There is no right answer, there may be better answers, but there is no absolute right answer for each patient.Chu We are going to have an opportunity to get in depth about the treatments that both of you have to offer to patients, but let me ask about a different group, who are the men that you would consider watchful waiting for?Peschel A typical patient that we would think about watchful waiting for would be an elderly patient, perhaps in their late 70s, a patient with severe medical problems,

heart disease, lung disease, kidney disease, and a life expectancy less than 10 years, they would be good observation patients; also patients with low Gleason scores. The scoring system goes from 2 to 10. If you see a patient with a Gleason of 5 or 6, we usually would discuss observation with that particular patient. It is like you know them when you see them, and observation is a perfectly good option for many of the patients that we see.11:17 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Dec-07-08.mp3Colberg There is even growing evidence and people are trying to define someone who has maybe a low volume, very localized disease, and that is the hard part. Even younger men could be considered for that protocol, but it is a very intense protocol meaning they follow up with you four times a year with PSA levels, rectal examinations, they get repeat biopsies at a year or 18 months to see and make sure that you actually do have low volume disease. We are not saying they are never going to be treated, but there may be a delay of treatment so that 6 months or a year down the road, they may be treated as opposed to immediately, but it is a very, very tricky dilemma to propose.Peschel There is some risk involved, the needle biopsy, which is what you are trying to make a decision on, is about 10% to 15% inaccurate. There could be a higher grade tumor hiding somewhere that the biopsy did not see. Secondly, the tumor can transform itself from a very low-grade to a higher grade after two, three, or four years. Many patients need to have repeat biopsies to keep track of that.Miller Is there ever a role for imaging of the local prostate disease, such as with CAT scans or MRIs? Typically you do not use that as part of the evaluation process.Colberg If you look at men who have PSAs under 10 and Gleason scores of less than 8, the yield of bone scans and CAT scans and MRIs are pretty low. The way I use, for example the rectal MRIs or MRIs, is to look at the local disease. If someone is on the border, maybe he would be a good surgical candidate but you are not certain, maybe there is disease outside the prostate gland, maybe their PSA is 15 and they may have Gleason 8, sometimes an MRI will make the difference in suggesting he have surgery versus having radiation therapy.Peschel I think the role of other diagnostic tests is less important because the PSA is such a good screening tool. They are picking patients up who have very early disease, microscopic disease, and generally a CT scan or MRI scanner all that is useful for the average patients. It is very important for the patient between choosing surgery or radiation, but not so important in terms of staging.Colberg I think that in the next 5 to 10 years we are going to come up with a better imaging spectroscopy, ways to identify small or microscopic disease within the gland that you could do some focal therapy with, or find that person who has really low volume disease that you want to follow, but we are not quite there yet.Miller In breast cancer, we went from radical mastectomy to modified radical, and now to lumpectomy, and even the idea of very localized radiation to a part of the breast, do you see that happening in prostate cancer?14:16 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Dec-07-08.mp3Colberg I think it will happen. It is just that we do not have the imaging technology or the capabilities yet, plus prostate cancer tends to be a multifocal disease so

that even if you have biopsies on one side, or one particular area, and when we take the prostate out, the disease will be in several areas of the prostate, so again it is a very tricky proposition but that is where we are headed.Peschel I agree with that. When I started treating prostate cancers 30 years ago, the vast majority of patients had disease outside the prostate at diagnosis; it had already spread before treatment. Now, probably 90% or more of the patients have the disease confined to the prostate. The exception is huge stage migration and I think the next step I agree with John, MRI spectroscopy can now plot the three-dimensional distribution of the tumor inside the prostate and it should be possible to use even more focal treatment rather than just treating the entire prostate.Miller That is very exciting. We are going to take a break now for a medical minute. We will be back with Dr. Richard Peschel and Dr. John Colberg from Yale Cancer Center talking about prostate cancer.Miller Welcome back to Yale Cancer Center Answers. This is Dr. Ken Miller and I am joined by my co-host Dr. Ed Chu and our guests Dr. John Colberg and Dr. Richard Peschel, who are experts in the treatment of prostate cancer. Let me ask you, for patients diagnosed with prostate cancer, who is on the multidisciplinary team and how do you use that team approach?Peschel We work very well together as a team, and John and I have developed the philosophy over time and we are very, very comfortable in terms of deciding who gets surgery and who gets radiation. Kevin Kelly, in medical oncology, is also part of that team. We have a conference that meets twice a month to16:52 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Dec-07-08.mp3 discuss difficult patients. There is a large, wide spectrum of expertise that is involved in helping patients make a decision.Colberg Often times these patients, even though they may have surgery or they may have radiation therapy, often times they may need other things. They may need radiation therapy after their surgery, they may need hormonal therapy, so it is more of a multidisciplinary approach to all these cancers, not only prostate but all of the GU cancers.Chu As you were saying earlier John, the decision to undergo a certain treatment is very individualized. I know all of us have friends and colleagues who have had early stage prostate cancer and have gone through the anxiety of trying to determine whether or not they should undergo surgery versus radiation therapy. Maybe you can take us through the pros and cons, advantages and disadvantages, from your advantage point? John, we can start off with you.Colberg Well as you know I do the surgery, but I am fairly open about it and I try to give the patients all the options. In general, we operate on younger more healthy patients, now that does not mean we do not operate on a 70-year-old man, we do, but in general terms, that is the first thing you look at, then you look at the stage of disease. You want to operate on localized prostate cancer, people who do not have disease outside the prostate, and that is based on patient examination, the patient's PSA level and pathology, the Gleason score, which you have talked about several times, and then ultimately my role is to give the patient as much information as I can. A lot of men come in with an idea of what they want to have done and they are just confirming or determining if it's the person they want to take

care of them, but often times we will send patients back and forth between Dr. Peschel and myself. I'll have a patient I think is a surgical person, but just to circle the wagons and make sure he is comfortable with everything I'll send him to Dr. Peschel and he will talk with him about radiation therapy.Peschel Obviously a big concern that either is, or is not discussed, but clearly is in the forefront of a lot of males' minds, is this is issue of sexual function after surgery and the high risk of impotence.Colberg There are two big down sides of surgery, and for radiation one is the same, and that is a loss of sexual function or erectile dysfunction and incontinence, the inability to control your urine after the operation. Those are very, very concerning issues, not that they can't be handled if you develop those after surgery, but certainly that is a big concern of all the patients, and if you look at surgery, for someone who does a safe number of radical prostatectomies a year, you are talking in the sense of incontinence of anywhere from 3% to 5%. Erectile dysfunction or sexual dysfunction is based on two things, the age of the19:57 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Dec-07-08.mp3 patient and what their status is before the operation. If you have a 50-year-old man who has good erections before the operation, your success rate with surgery if you do nerve sparing is probably somewhere between 70% to 80%. If you are 70 years old and you have fair erections, it is probably more like 10% or 20%.Miller I want to ask the same thing with radiation, because again these are the issues that men are going to be asking about. If you treat a man with radiation and he has the same issue as that 50-year-old and 70-year-old man, what are the risks?Peschel The question with radiation therapy is that most of our patients who have more advanced disease, higher grade, will also receive hormone therapy, and the combination of hormone therapy and radiation therapy produces more erectile dysfunction than that of just radiation therapy alone. For those that just get radiation, erectile dysfunction is about 20% to 30%, very similar to surgery, but we need to use hormones in many patients and the impotence rate climbs to about 50%.Chu It is interesting because I think the general misconception is that with radiation therapy there is no risk for developing erectile dysfunction.Peschel Yeah, there are a couple of components to that. One of them I mentioned, the use of hormone therapy definitely adds to erectile dysfunction, and secondly, our age group is older; our average patient is about 70 to 78 years old. Surgical patients are said to be younger, so they have fewer age factors in terms of whether they'll be potent or not.Chu And with surgery people will not immediately be potent after the operation, it may take six months to 12 months to actually recover their sexual function.Peschel To be honest with you, the data documenting potency sparing is very poor. It is very soft data. There are not really any good studies, so when we talk about these numbers, they are very soft numbers.Chu Have the complications secondary to radiation therapy improved now that you are developing more sophisticated focused approaches to deliver the radiation therapy to patients?Colberg Yes, the complication rights have fallen dramatically. This intensity-modulated radiation therapy, which we have used at Yale for over 10 years, has produced complication rates that

are the lowest we have ever seen. All other types of radiation therapy that we used in the past for prostate cancer produced 6% to 15% complications that affected quality of life. With IMRT, based on 800 patients that we have treated, it is down to less than 1%, we've just never 22:43 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Dec-07-08.mp3 seen anything like it. Now we are moving into what is called image-guided intensity-modulated radiation therapy, which should allow us to escalate the dose more but maintain these very low complication risks.Miller Since we are talking about radiation, can you tell us a little about seed implants, what are they and who should receive that treatment?Colberg We used to do a lot of seed implants; I have done 500 myself. It is the placement of little tiny radioactive seeds into the prostate in a set distribution to produce a minimum dose to the outside of the prostate. There are two different isotopes that are used; one is iodine-125 and the other is palladium-103. We have tended to use palladium here at Yale because of the shorter half-life. In an amazing way, we have set aside prostate implant at Yale because our intensity-modulated radiation therapy results are so good, the complication rate is 1/10th that of implant, and the cure rates look better than with implants, so we have tended to emphasize in our patient population intensity-modulated radiation therapy.Peschel John, as we have been talking about the advances in radiation therapy, there also have been some pretty significant advances in surgical techniques.Colberg The most recent advance is the idea of minimally invasive prostatectomy using a system called the da Vinci System, which is a robotic-type system. It has been around since early 2001-2002. In that time, there have been around 400 prostates done that way. In the United States now, probably 50% of all prostatectomies are done robotically. In the next five years, 80% or 90% will be done robotically. What the system is, is it operates through small little punctures in the lower abdomen, in fact we make about six little holes in the abdomen, and through these little holes we have a camera and working ports where you are actually able to operate this robot remotely from across the room and do the same operation. The advantages are several; one, less blood loss, less time in the hospital, less pain, and less time with the Foley catheter. As far as the important things of prostatectomy, such as cancer control, it seems to be equivalent to open operation. Potency may be a little bit better and the return of erectile erections may be back sooner with the robotic prostatectomy. And with incontinence, it may be about the same at a year, but may also be controlled a little bit sooner. We have had the machine, the robotic system, at Yale for about two plus years, and I would say 95% of our patients have robotic prostatectomies. There is always a rare instance where you need to still do an open procedure, and there is always a risk when you do robotic prostatectomies that it may need to be converted to an open operation because they can't be done robotically, but it is very exciting.25:49 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Dec-07-08.mp3Miller I want to ask you, John, because you have done both kinds of procedures, for you as a surgeon, what is it like on the other side of the room?Colberg Certainly there is a learning curve to the procedure. It is not a huge learning

curve for someone who has done a lot of open operations and is very adept at laparoscopic skills, but it is a different operation, it has much better visualization and you see things that you probably did not see before. The way you dissect things is more exact, dissect the nerves and preserve the sphincter for the urethra, so I think that it is a very good operation and is definitely here to stay.Chu Is this robotic surgery just for prostate cancer, or potentially could it be applied for surgical resection of other tumors?Colberg Certainly they use it for a lot of different tumors. They can use it for a pediatric population for pyeloplasties, obstructions in the kidney, people have done it for partial nephrectomies, radical nephrectomies, general surgery has used it for distal pancreatectomies, colon resections, thoracic uses it, cardiovascular uses it for mitral valve repairs, urology will use it eventually and people are already using it to remove bladders for radical cysto-prostatectomies. It is just beginning to take off as far as what it can be used for.Peschel The good news about this procedure is that John has appropriately advanced the age where patients can have surgery. The average age of patients having surgery used to be 58, and I think John pushes that up to 68 or 69, so it gives older patients the opportunity to think about the surgical option.Miller A man comes to you who is 50 years old, let us say, with a PSA that is 3 or 4 and an intermediate Gleason's grade. I am trying to paint a high risk, and not a low risk patient, and he says to you, "What is better, should I have radiation or should I have surgery?" How do you answer that?Colberg We have developed a philosophy at Yale that the younger patients should be offered surgery. The reason for that is that an average 50 year old will live 25 years easily, and you need to look at the long-term data and the long-term data for surgery is more robust and it is better defined. So we really emphasize surgery in the very young patients.Chu Is there ever any role after surgery for additional radiation therapy plus or minus hormonal therapy?Colberg That is a great question and that comes up for a lot of patients. With PSA it tempers it a bit because if you have a prostatectomy and your PSA becomes undetectable or zero, there is no evidence of disease. What happens to the man28:54 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Dec-07-08.mp3whose PSA starts to go up after surgery? That gets to be a very difficult dilemma because there are certain parameters you are going to look at, when did the PSA go up, what did the original pathology show? Maybe Dick can describe what our philosophies are on who we radiate.Peschel There are two programs, one is called adjuvant radiation therapy, if you see poor pathologic findings at surgery you immediately treat the patient with post-op radiation therapy. The other is called salvage radiation therapy where you wait for the patient's PSA to become detectable and then treat with post-op radiation therapy; the two are very different approaches.Chu You have been listening to Yale Cancer Center Answers and we would like to thank our guest experts, Dr. John Colberg and Dr. Richard Peschel for joining us. We look forward to having you back on a future show. Until next time, this is Dr. Ed Chu from the Yale Cancer Center wishing you a safe and healthy week.If you have any questions for the doctors or would like to share your comments, go to www.yalecancercenter.org

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