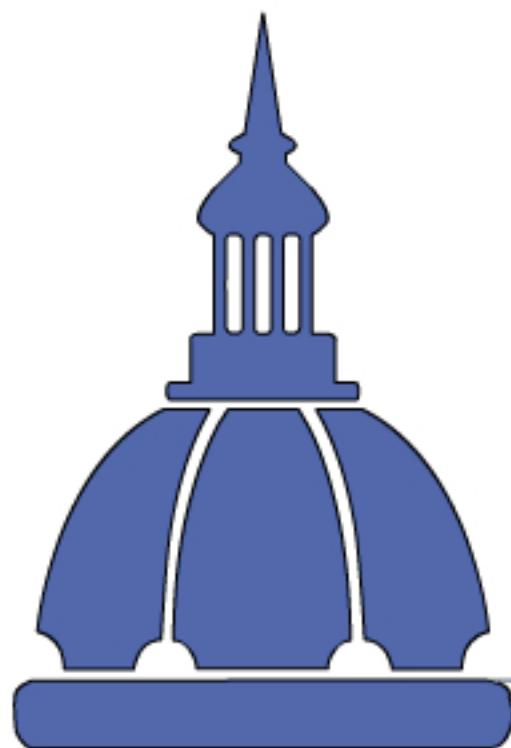


Introduction



The Sol Goldman
Pancreatic Cancer Research Center

Welcome.

This animation was designed for the Johns Hopkins Pancreas Cancer website to offer some new information about the early precursors to pancreatic cancer.

We will show how an understanding of these precursors and the changes that they produce in the pancreas could lead to a method for the early detection of this devastating illness.



Start

Pancreas
Anatomy

What are
Precursor
Lesions?

Effects
on the
Pancreas

EUS
Screening

Saving
Lives



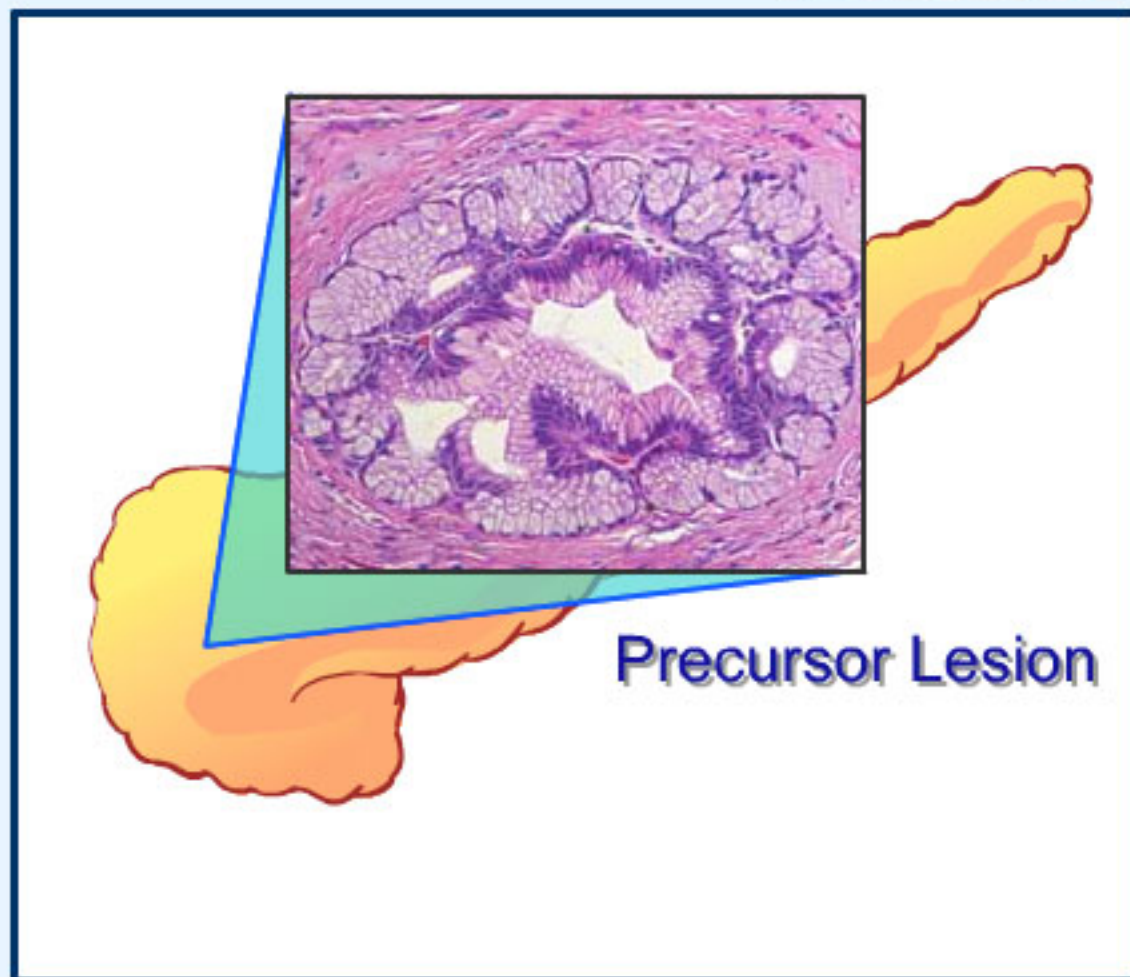
Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Introduction



Pancreatic cancer is difficult to treat, in large part because most patients are not diagnosed until after the cancer has already spread beyond the pancreas.

Significant progress has been made, however, in understanding the precursor lesions that give rise to invasive pancreatic cancer. These precursor lesions have become exciting new targets for early detection efforts.



Start

Pancreas
Anatomy

What are
Precursor
Lesions?

Effects
on the
Pancreas

EUS
Screening

Saving
Lives



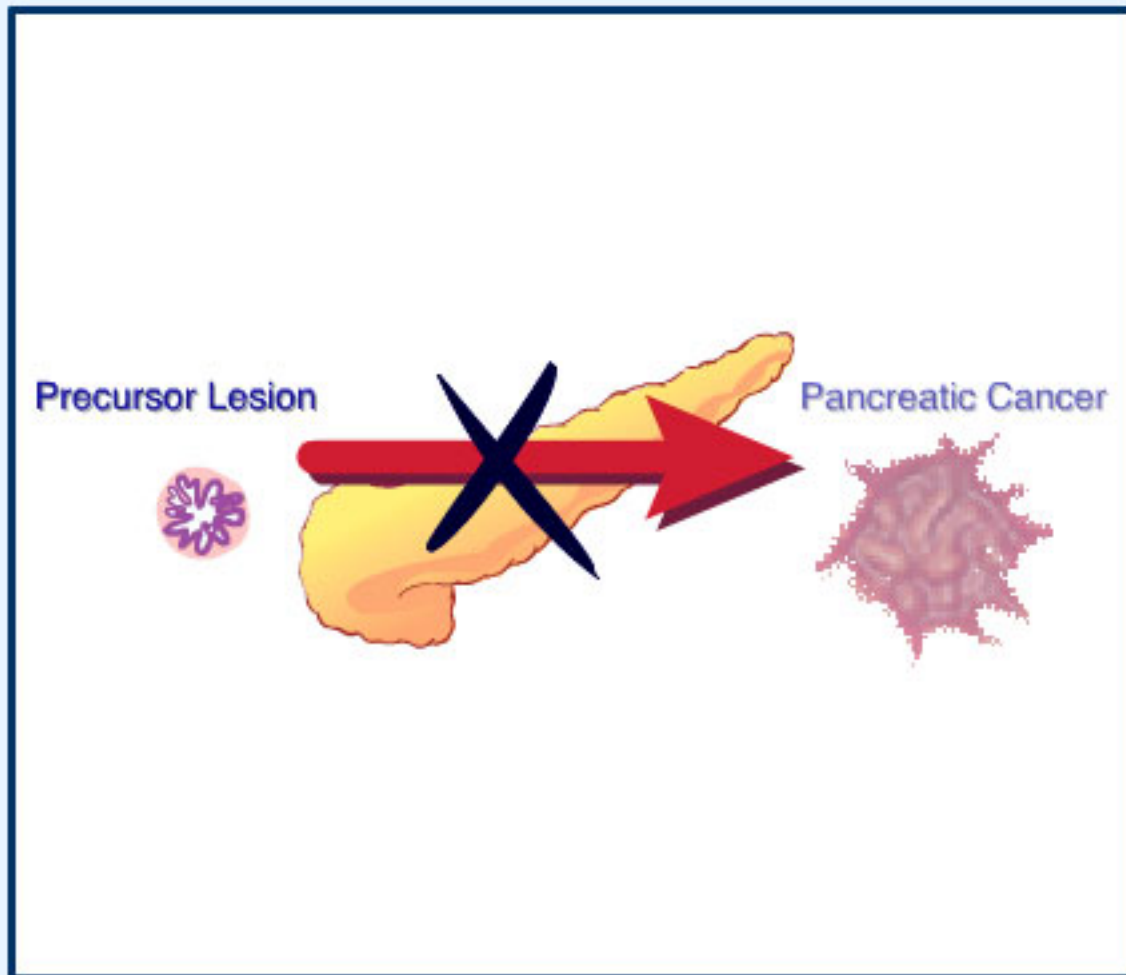
Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Introduction



Just as colon polyps, if left alone, can give rise to a colon cancer, so too is it now clear that small treatable precursor lesions are present in the pancreas years before invasive pancreatic cancer ever develops.

The identification and treatment of these noninvasive precursor lesions in the ducts of the pancreas offers the potential to prevent invasive pancreatic cancer.

[Start](#)[Pancreas Anatomy](#)[What are Precursor Lesions?](#)[Effects on the Pancreas](#)[EUS Screening](#)[Saving Lives](#)

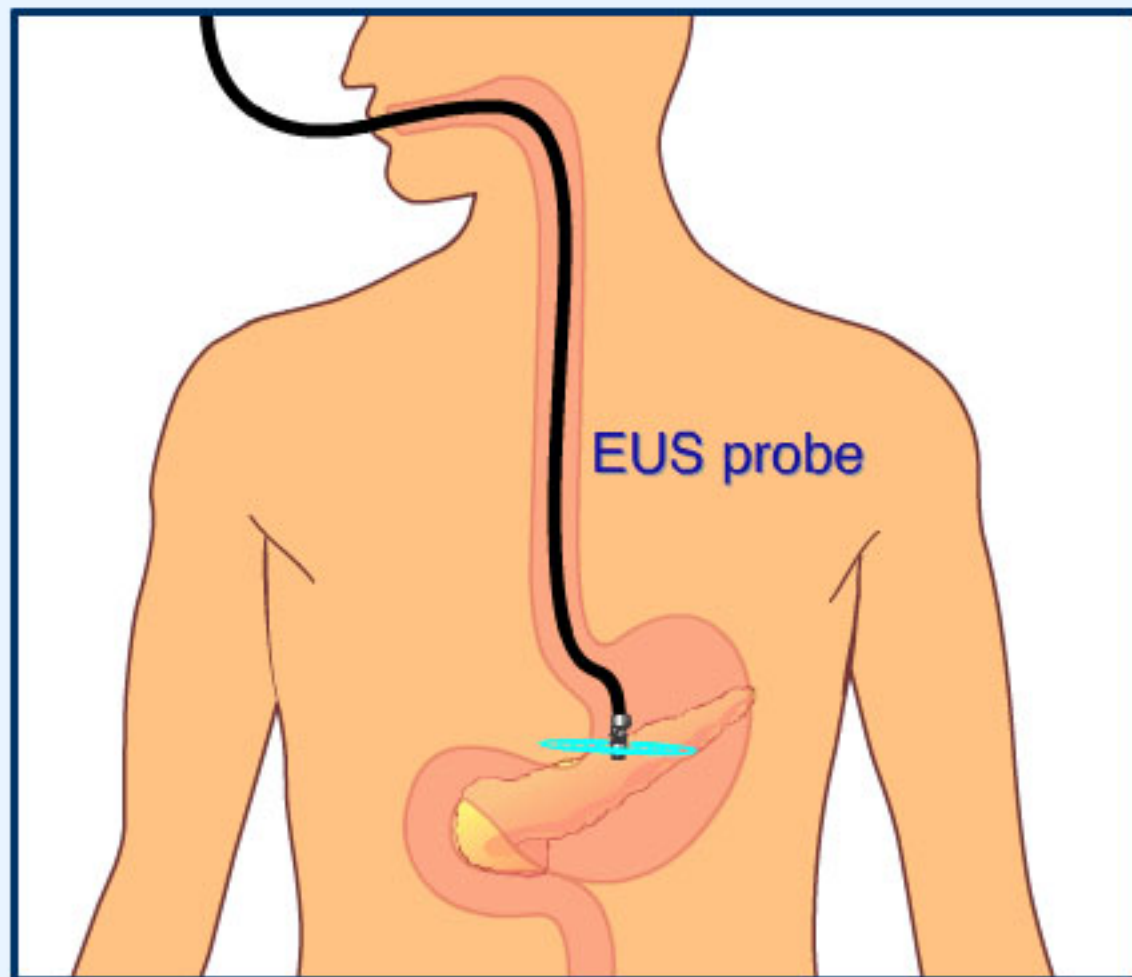
Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Introduction



The precursor lesions associated with most pancreatic cancers are microscopic in size and virtually impossible to detect with traditional imaging methods.

However, recent discoveries at Johns Hopkins regarding the effects of these precursor lesions on the pancreatic tissue, combined with the development of endoscopic ultrasound (EUS), offer the potential for early detection, especially with patients known to have a greater risk of developing pancreatic cancer.

[Start](#)[Pancreas Anatomy](#)[What are Precursor Lesions?](#)[Effects on the Pancreas](#)[EUS Screening](#)[Saving Lives](#)

Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Introduction

- 1
Anatomy of the Pancreas
- 2
What are Precursor Lesions?
- 3
How do Precursor Lesions
Affect the Pancreas?
- 4
Detecting Precursor Lesions
Using EUS

First, let us review the anatomy of the pancreas. We will then learn about precursor lesions and observe how these precursor lesions produce visible changes in the pancreas.

Finally, we will see how the understanding of these changes in the pancreas could lead to methods for early diagnosis using endoscopic ultrasound (EUS).

[Start](#)[Pancreas
Anatomy](#)[What are
Precursor
Lesions?](#)[Effects
on the
Pancreas](#)[EUS
Screening](#)[Saving
Lives](#)

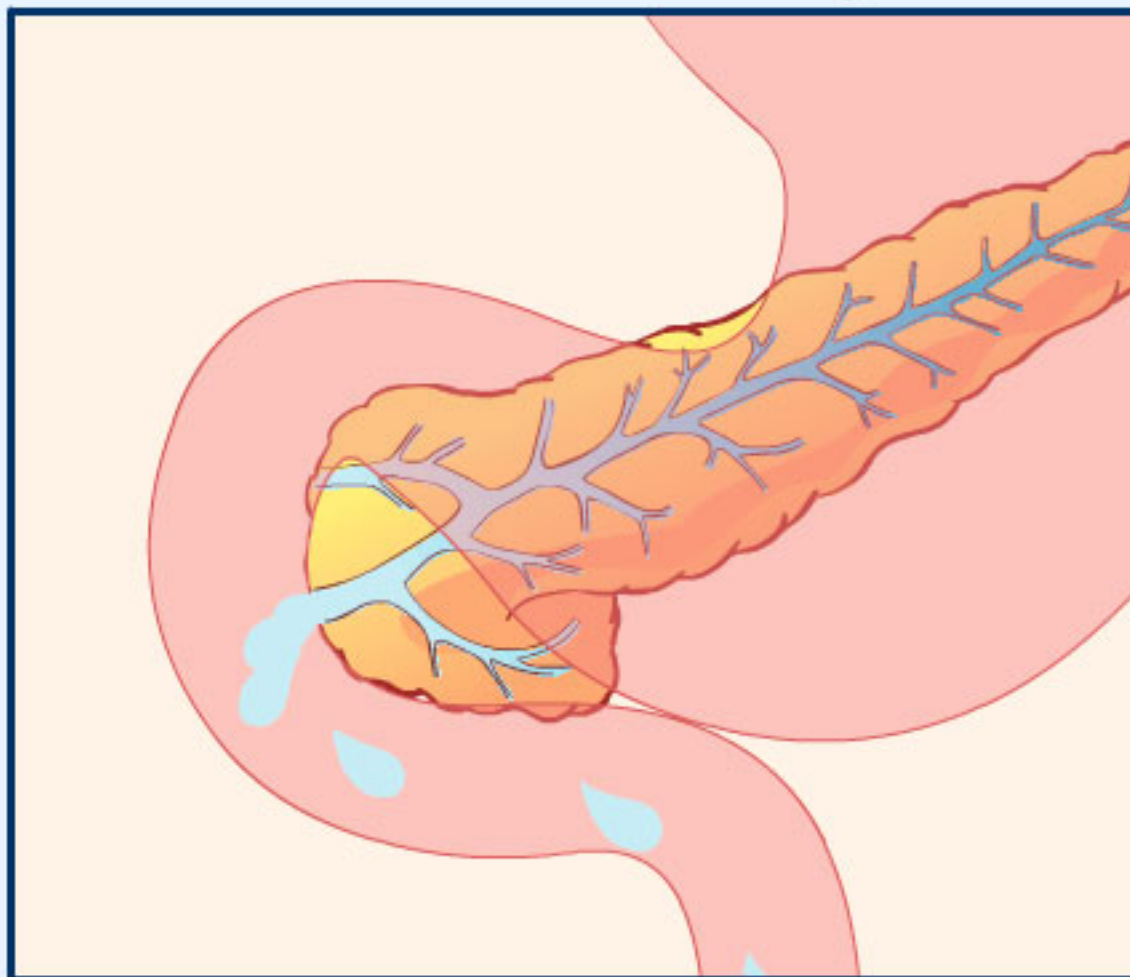
Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Anatomy of the Pancreas



The pancreas is an elongated gland that lies behind the stomach, in close proximity to the first part of the small intestine, the duodenum.

Pancreatic tissue is made of many small collections of cells called lobules and a system of branching ducts.

The ducts are essentially small tubes that transport fluids made by the pancreas to the duodenum.

[Start](#)[Pancreas Anatomy](#)[What are Precursor Lesions?](#)[Effects on the Pancreas](#)[EUS Screening](#)[Saving Lives](#)

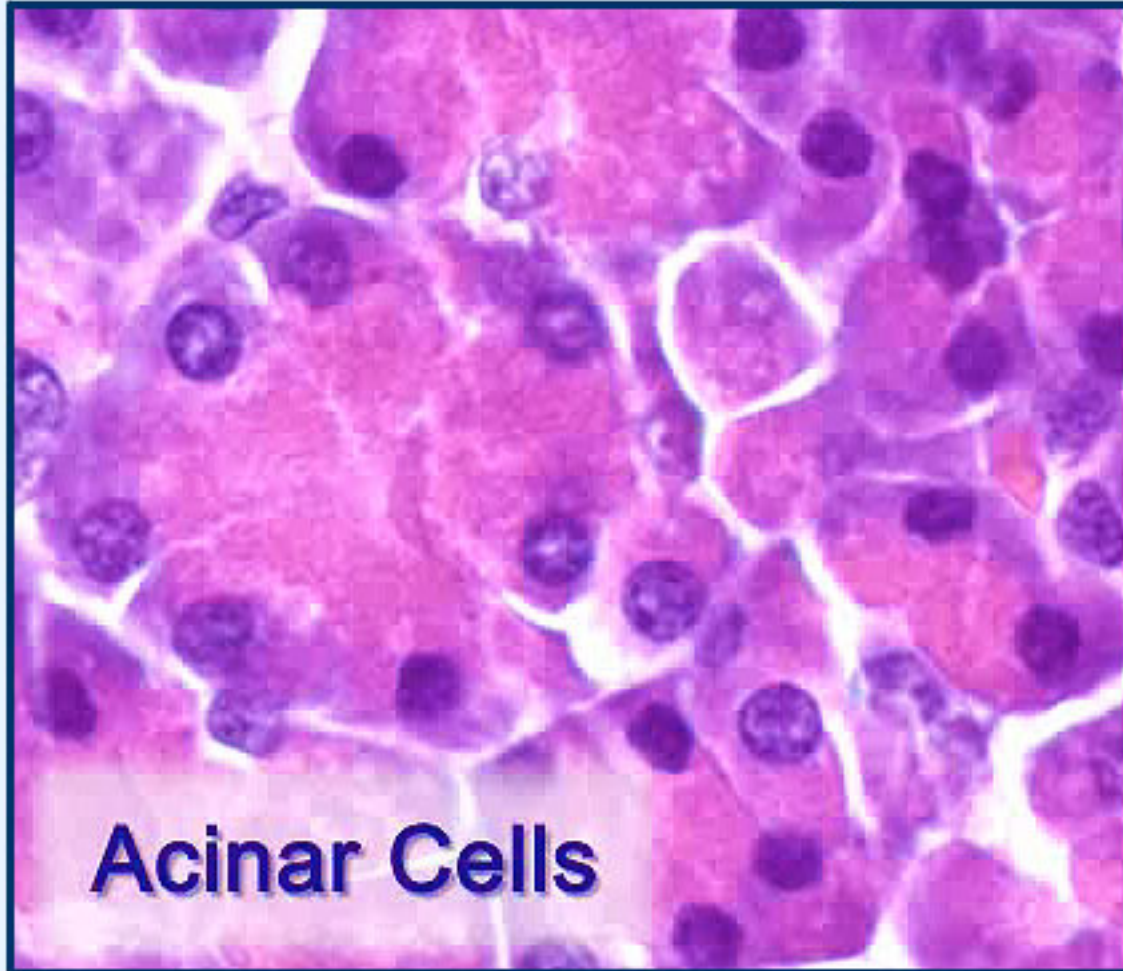
Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Anatomy of the Pancreas



Under the microscope, we see that the healthy pancreas is fairly homogeneous in appearance. The lobules are mostly made up of cells called acinar cells. These cells are the exocrine part of the pancreas. They are arranged in grape-like clusters called acini.

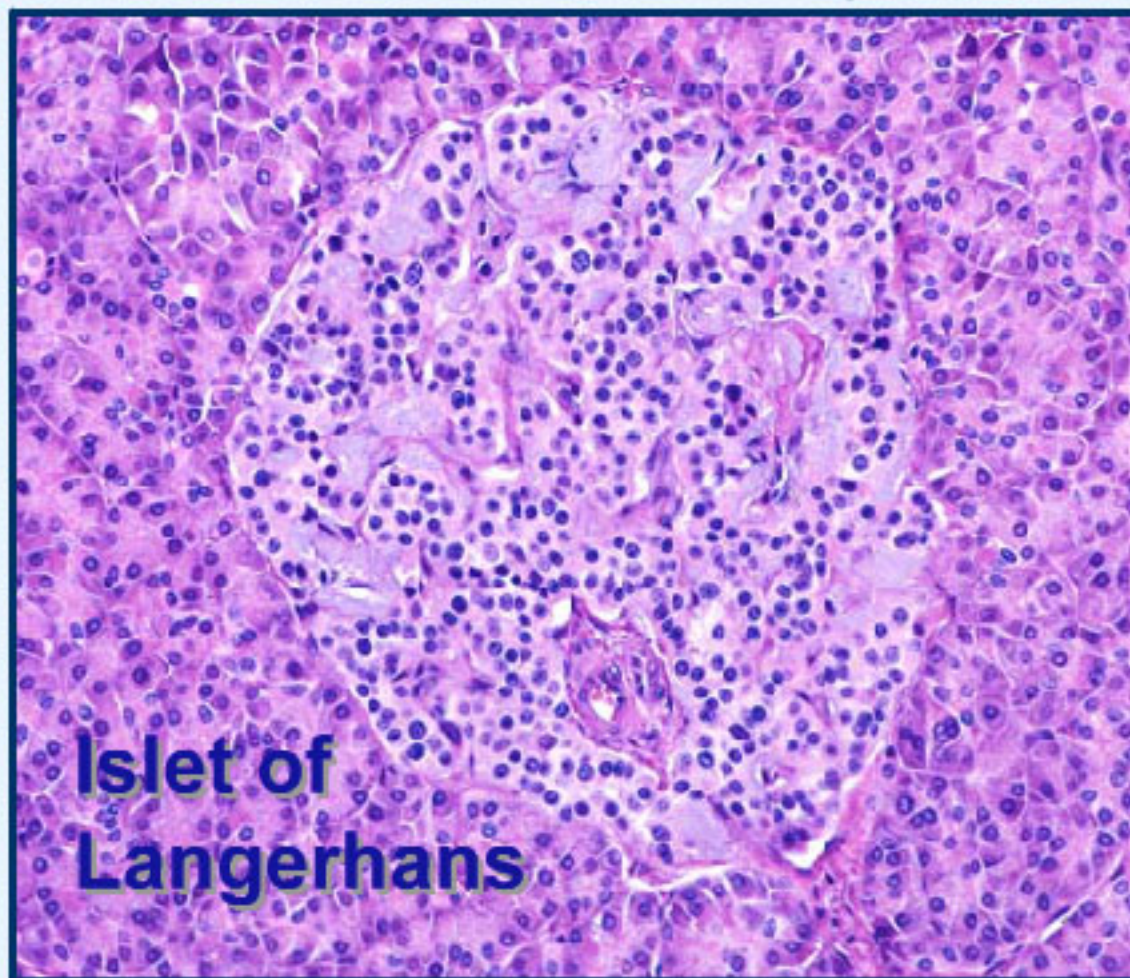
The acinar cells make pancreatic juice that travels through the duct system of the pancreas into the duodenum. In the duodenum, this pancreatic juice helps us digest our food.

[Start](#)[Pancreas Anatomy](#)[What are Precursor Lesions?](#)[Effects on the Pancreas](#)[EUS Screening](#)[Saving Lives](#)

This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Anatomy of the Pancreas



Scattered evenly throughout the pancreas are small clusters of endocrine cells called the Islets of Langerhans.

These cells produce the hormones that control our blood sugar levels. These hormones are released directly into the blood vessels of the pancreas.

The Islets of Langerhans and the acini group together to form uniform lobules, each supplied by a branch of the duct system.

[Start](#)[Pancreas Anatomy](#)[What are Precursor Lesions?](#)[Effects on the Pancreas](#)[EUS Screening](#)[Saving Lives](#)

Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

What Are Precursor Lesions?

Understanding the biology of precursor lesions is of great importance in order to learn how to detect and potentially treat pancreatic cancer before it becomes invasive and spreads.



What are Precursor Lesions?

[Start](#)[Pancreas Anatomy](#)[What are Precursor Lesions?](#)[Effects on the Pancreas](#)[EUS Screening](#)[Saving Lives](#)

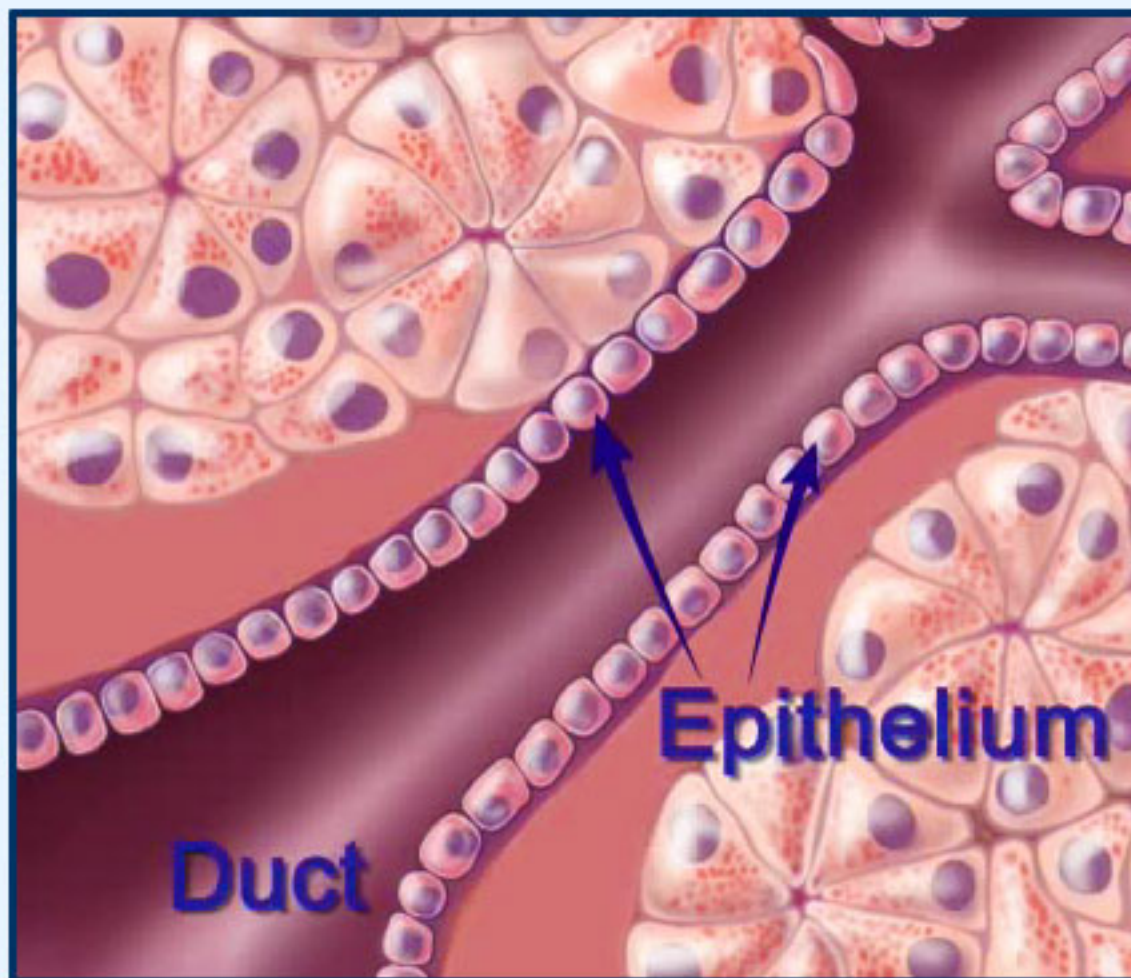
Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

What Are Precursor Lesions?



Fundamentally, a precursor lesion is an abnormal change in the layer of cells lining the ducts of the pancreas.

This layer is called the epithelium.

The epithelium of a healthy pancreas consists of short, uniform, cube-like epithelial cells.



Start

Pancreas
Anatomy

What are
Precursor
Lesions?

Effects
on the
Pancreas

EUS
Screening

Saving
Lives



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

What Are Precursor Lesions?



A precursor lesion occurs when a genetic mutation causes the epithelial cells to change and grow too fast. While these cells are growing too fast, they have not yet taken on all of the characteristics of invasive cancer.

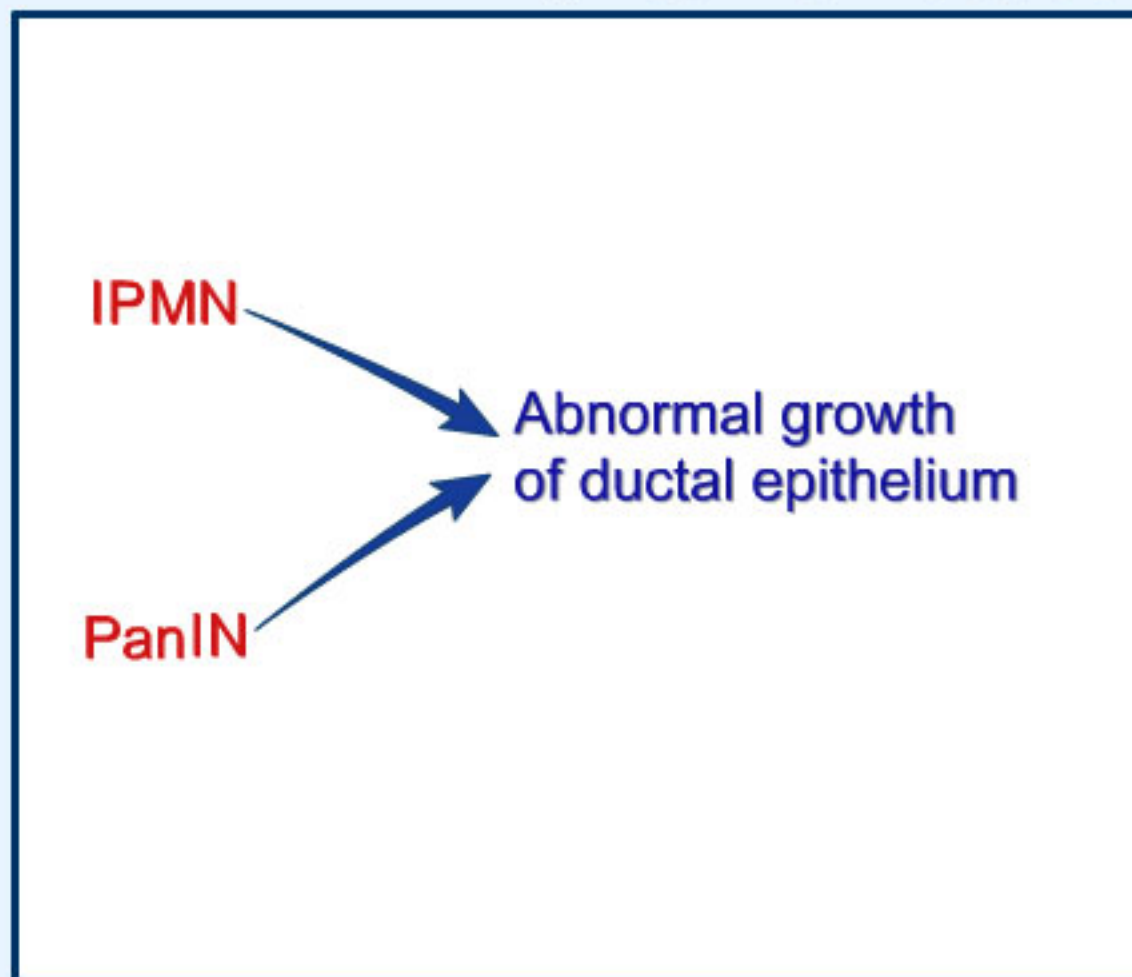
Specifically, they have not yet become invasive. They have not yet broken through the tough basement membrane that lines the normal ducts, and they therefore have not spread to the surrounding tissue.

[Start](#)[Pancreas
Anatomy](#)[What are
Precursor
Lesions?](#)[Effects
on the
Pancreas](#)[EUS
Screening](#)[Saving
Lives](#)

This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

What Are Precursor Lesions?



Two types of precursor lesions have been identified in the ducts of the pancreas: Intraductal Papillary Mucinous Neoplasms (IPMNs) and Pancreatic Intraepithelial Neoplasia (PanINs.) They both represent an abnormal growth of the epithelium lining the ducts.



Start

Pancreas
Anatomy

What are
Precursor
Lesions?

Effects
on the
Pancreas

EUS
Screening

Saving
Lives



Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

What Are Precursor Lesions?

IPMN



Big enough to see
Often produce symptoms

PanIN



Too small to see
No symptoms

IPMNs are generally larger than PanINs. They are found in the large ducts of the pancreas, they produce a lot of mucous and cause the ducts to expand. IPMNs are clinically detectable.

On the other hand, PanINs, the precursor lesions associated most closely with the development of pancreatic cancers, are much smaller, almost the size of the head of a pin. Patients with PanINs show no clinically observable symptoms.



Start

Pancreas
Anatomy

What are
Precursor
Lesions?

Effects
on the
Pancreas

EUS
Screening

Saving
Lives



Audio off

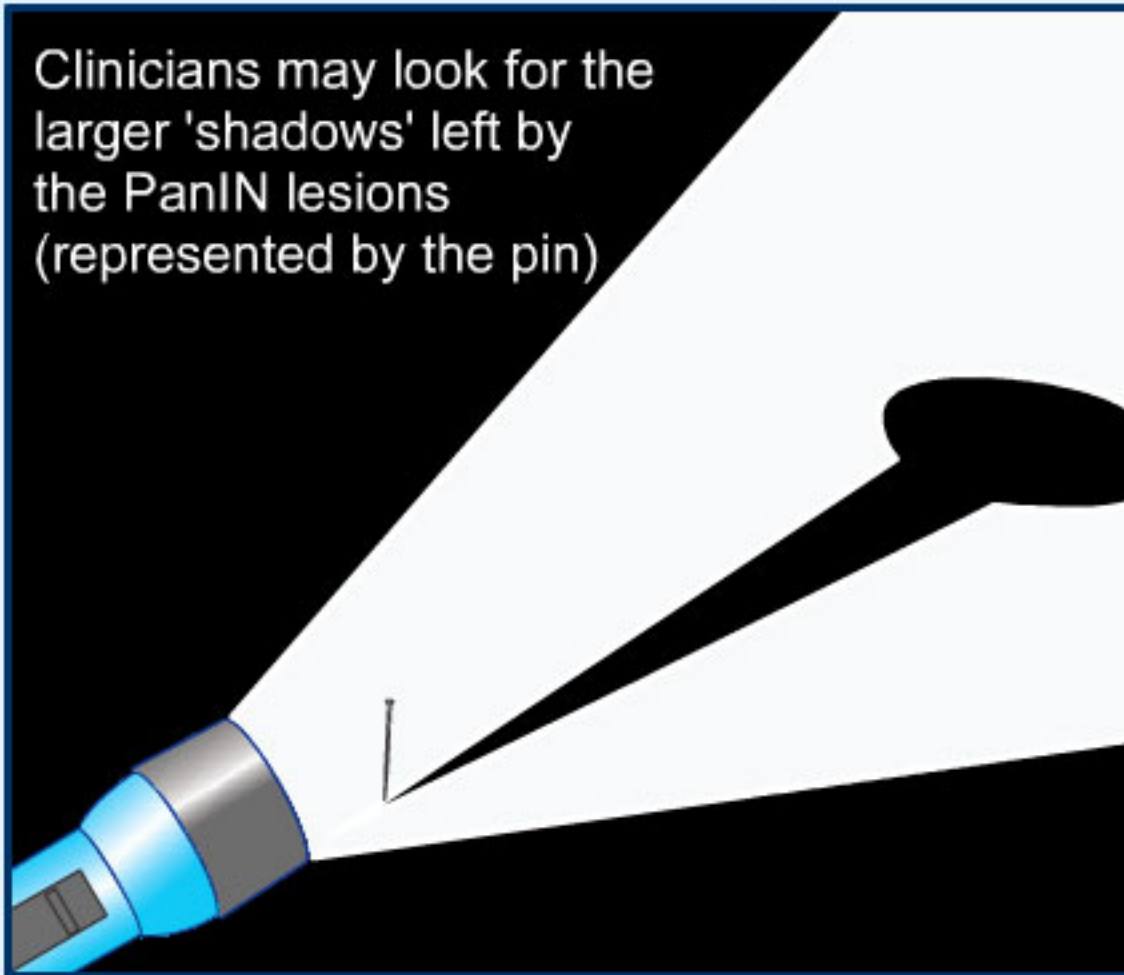


This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

What Happens to the Pancreas?

Clinicians may look for the larger 'shadows' left by the PanIN lesions (represented by the pin)



While PanINs are virtually undetectable because of their microscopic size, the distinctive traces that they leave on the pancreas are more easily detected. You might think of it as a small object casting a large shadow.

Clinicians may look for these larger 'shadows' in the pancreas as evidence of PanINs. If this holds true, PanINs may be detected, and once detected, treated long before they ever become cancer.

[Start](#)[Pancreas Anatomy](#)[What are Precursor Lesions?](#)[Effects on the Pancreas](#)[EUS Screening](#)[Saving Lives](#)

Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

What Happens to the Pancreas?



PanINs arise in the smallest ducts of the pancreas.

Under the microscope, the cells in these ducts can be seen to become taller and instead of laying flat, they form finger-like projections into the center of the duct.



Start

Pancreas
Anatomy

What are
Precursor
Lesions?

Effects
on the
Pancreas

EUS
Screening

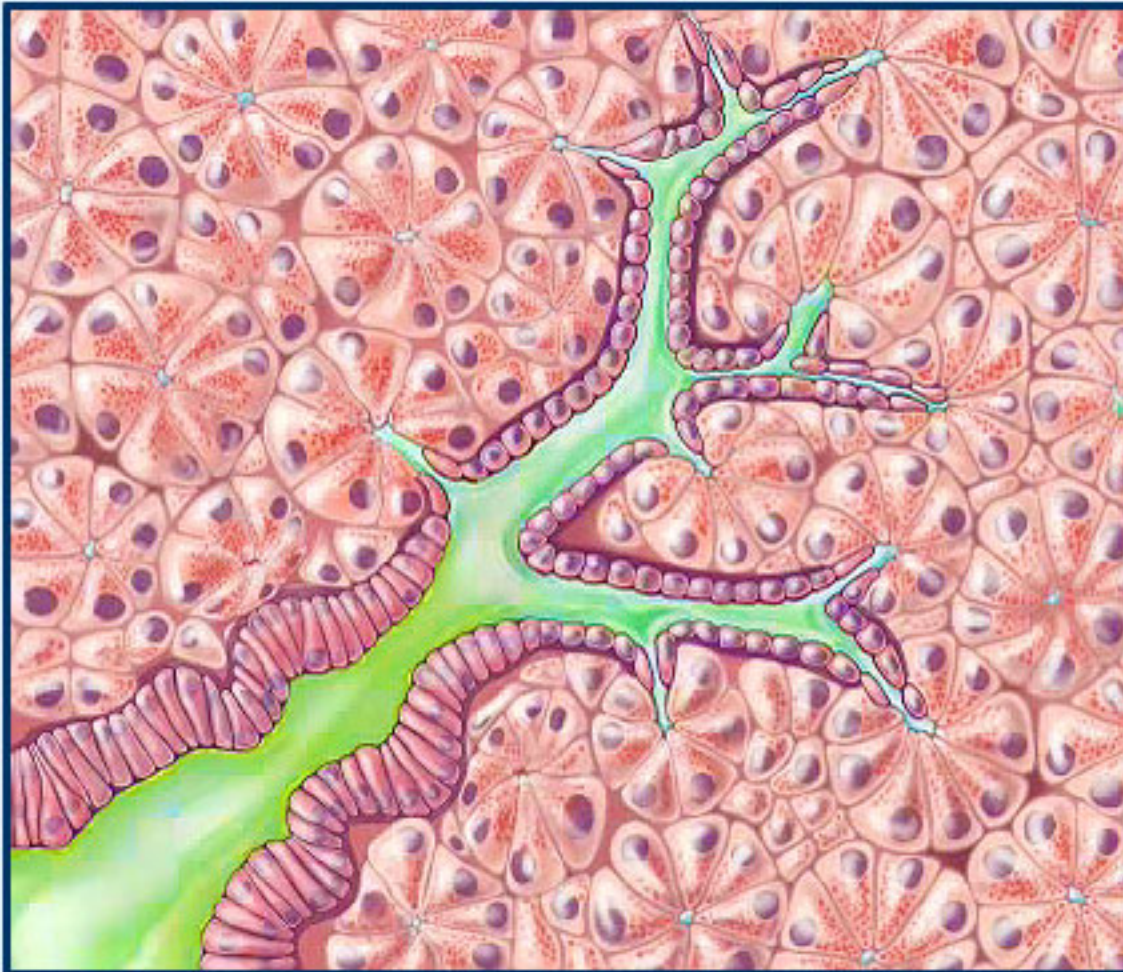
Saving
Lives



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

What Happens to the Pancreas?



Not only do the epithelial cells look abnormal under the microscope, but these cells also start to make proteins and types of mucous that they normally wouldn't make.

The altered mucous and proteins mix with the pancreatic juice, making it thicker and slowing down its flow through the ducts. Some studies suggest that one of the digestive enzymes produced in the pancreas may also be prematurely activated when it comes in contact with the PanIN lesion.

[Start](#)[Pancreas Anatomy](#)[What are Precursor Lesions?](#)[Effects on the Pancreas](#)[EUS Screening](#)[Saving Lives](#)

This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

What Happens to the Pancreas?



Whatever the cause, these lesions lead to damaging blockage of the ducts. This causes a distinct shrinkage, called atrophy, of the surrounding pancreatic tissue.

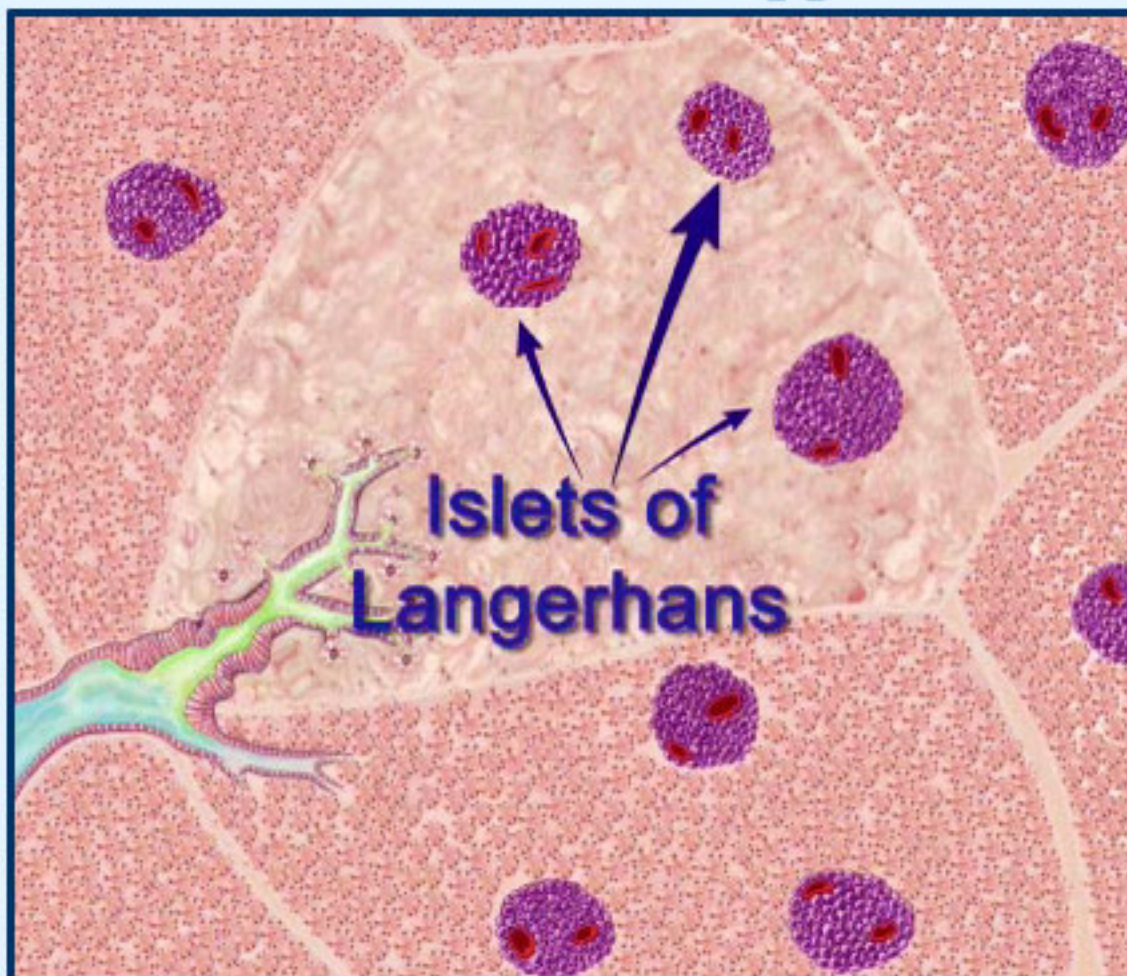
This atrophy begins with the disappearance of granules, which are normally seen inside the cells. The acinar cells then begin to shrink, causing much more noticeable spaces to appear in the center of each acinus.

[Start](#)[Pancreas Anatomy](#)[What are Precursor Lesions?](#)[Effects on the Pancreas](#)[EUS Screening](#)[Saving Lives](#)

This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

What Happens to the Pancreas?



The acinar cells recede and then many die off through processes that scientists call necrosis and apoptosis, or cell death. The space left behind is replaced with fatty or scar tissue.

All that remain of the healthy pancreas are the endocrine cells in the Islets of Langerhans.



Start

Pancreas
Anatomy

What are
Precursor
Lesions?

Effects
on the
Pancreas

EUS
Screening

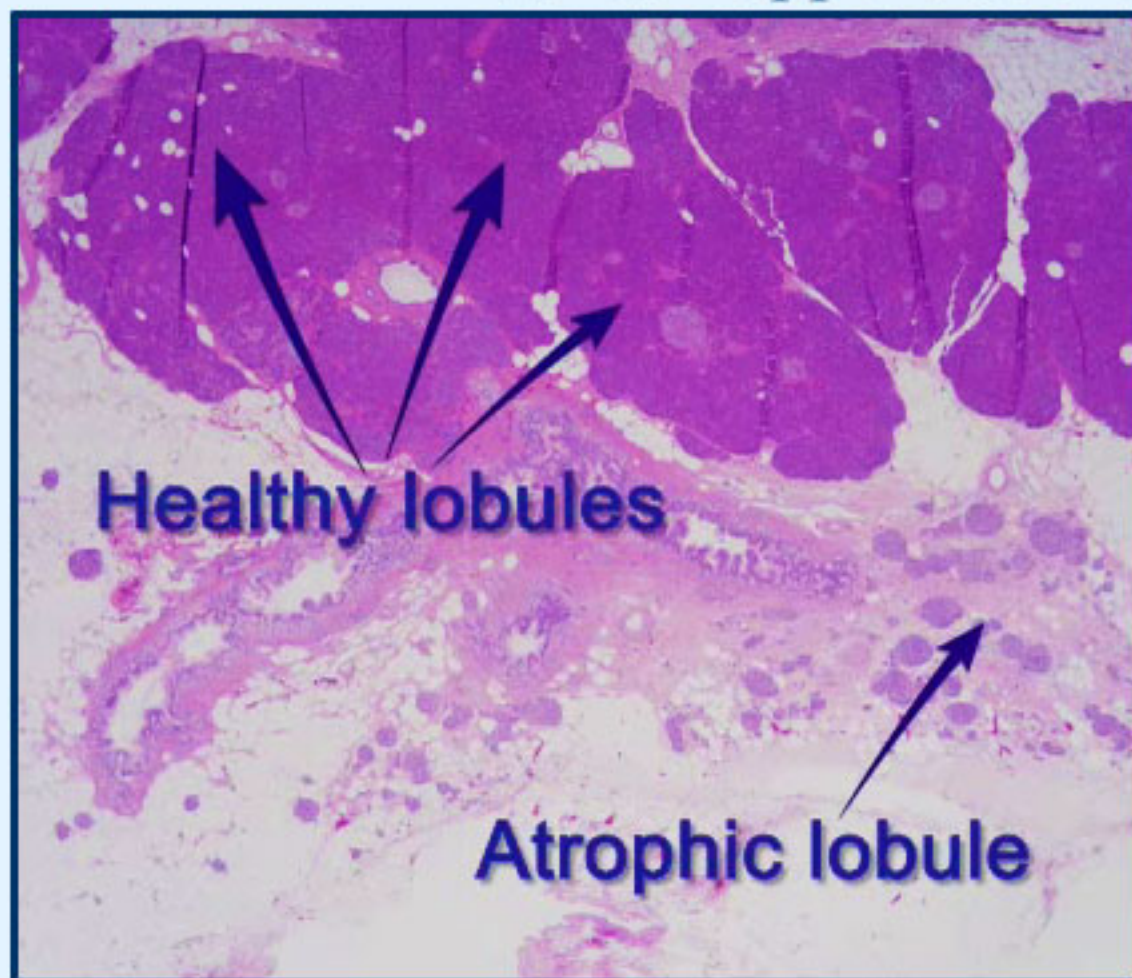
Saving
Lives



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

What Happens to the Pancreas?



Because only the portion of the pancreas 'upstream' from the PanIN lesion is affected, this atrophy is limited to single lobules within the pancreas.

Under the microscope, the normally homogeneous appearance of the pancreas is interrupted by atrophied lobules scattered randomly throughout the tissue, wherever a PanIN has formed.



Start

Pancreas
Anatomy

What are
Precursor
Lesions?

Effects
on the
Pancreas

EUS
Screening

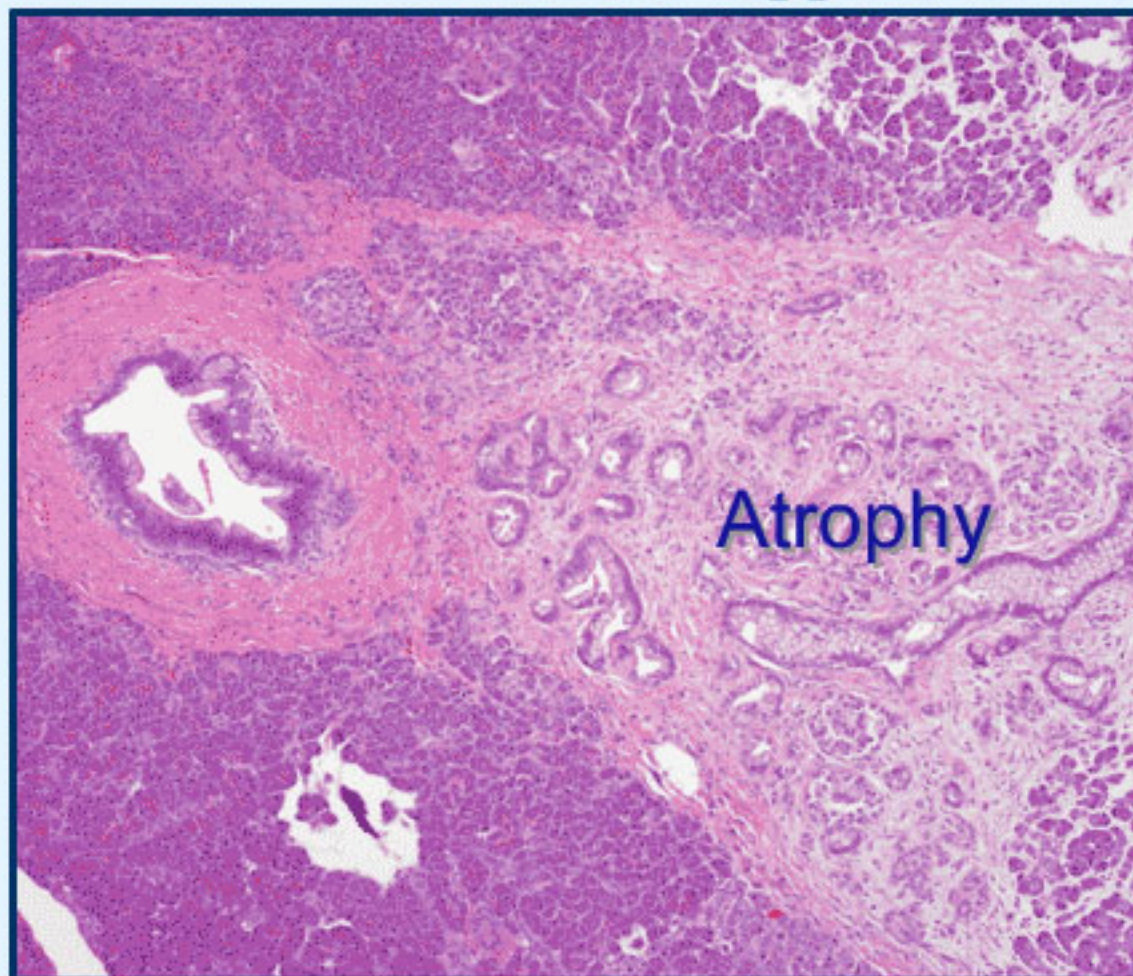
Saving
Lives



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

What Happens to the Pancreas?



These 'shadows' left by the PanIN lesions are much larger than the tiny PanIN lesions themselves. As a result, the areas of the pancreas atrophy can be seen using techniques such as endoscopic ultrasound, also called EUS.



Start

Pancreas
Anatomy

What are
Precursor
Lesions?

Effects
on the
Pancreas

EUS
Screening

Saving
Lives



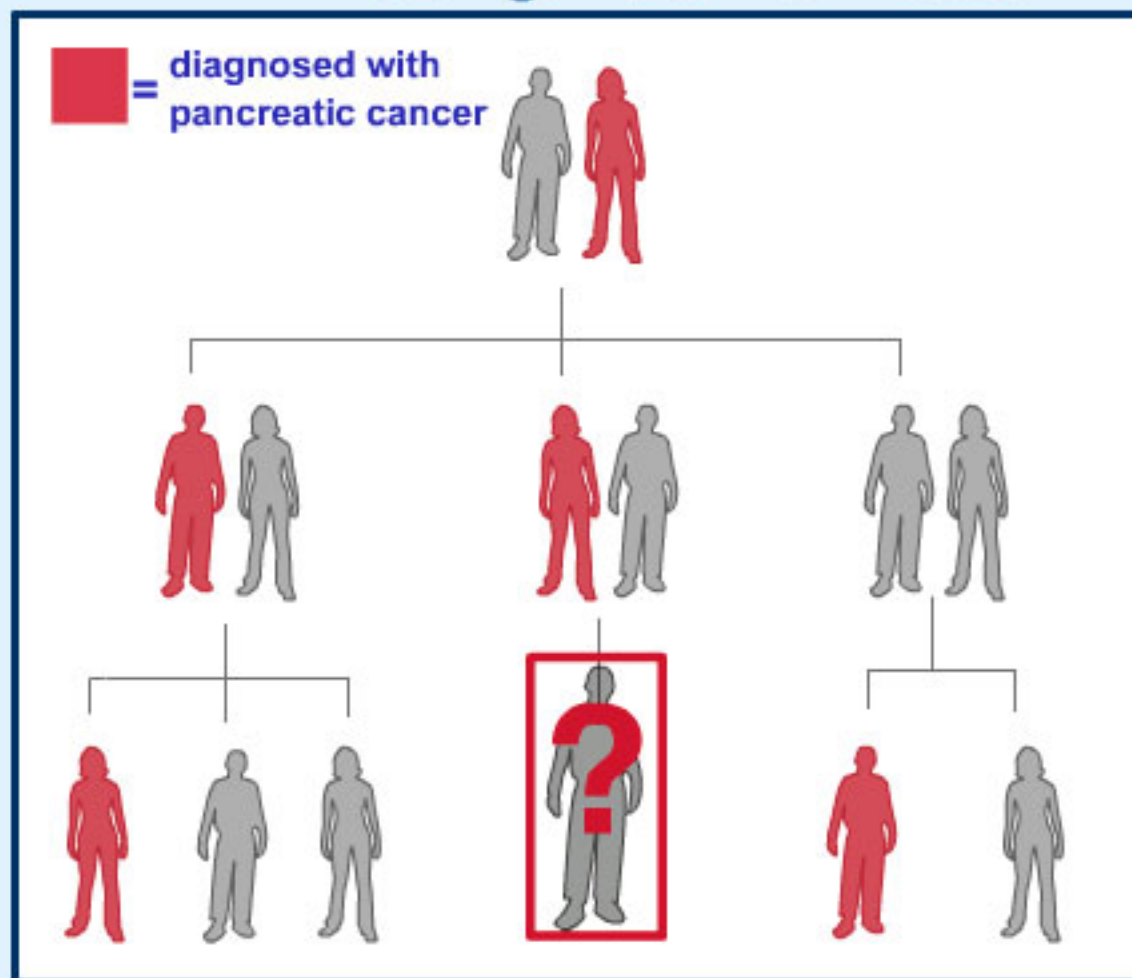
Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Using EUS To Detect Precursor Lesions



We now know that individuals with a strong family history of pancreatic cancer and individuals with certain inherited syndromes have an increased risk of developing pancreatic cancer.

We need to develop new tests to screen these individuals for precursor lesions so that they can be treated **BEFORE** an invasive cancer develops.

New methods for screening these individuals using EUS are currently being developed at Johns Hopkins.



Start

Pancreas
AnatomyWhat are
Precursor
Lesions?Effects
on the
PancreasEUS
ScreeningSaving
Lives

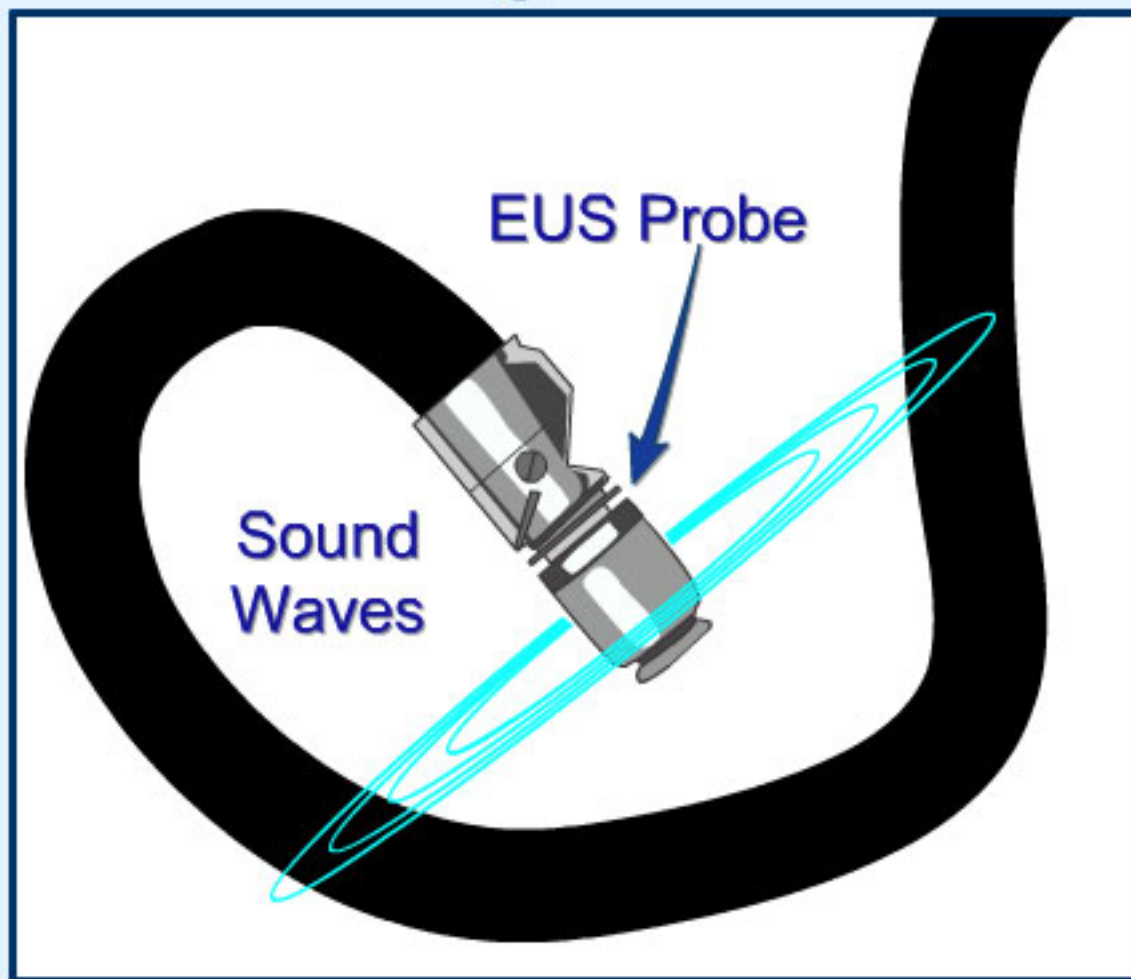
Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Using EUS To Detect Precursor Lesions



EUS, (or Endoscopic UltraSound), like traditional ultrasound, uses sound waves that create computer-generated images to visualize what lies within the body and to detect any abnormalities.

[Start](#)[Pancreas Anatomy](#)[What are Precursor Lesions?](#)[Effects on the Pancreas](#)[EUS Screening](#)[Saving Lives](#)

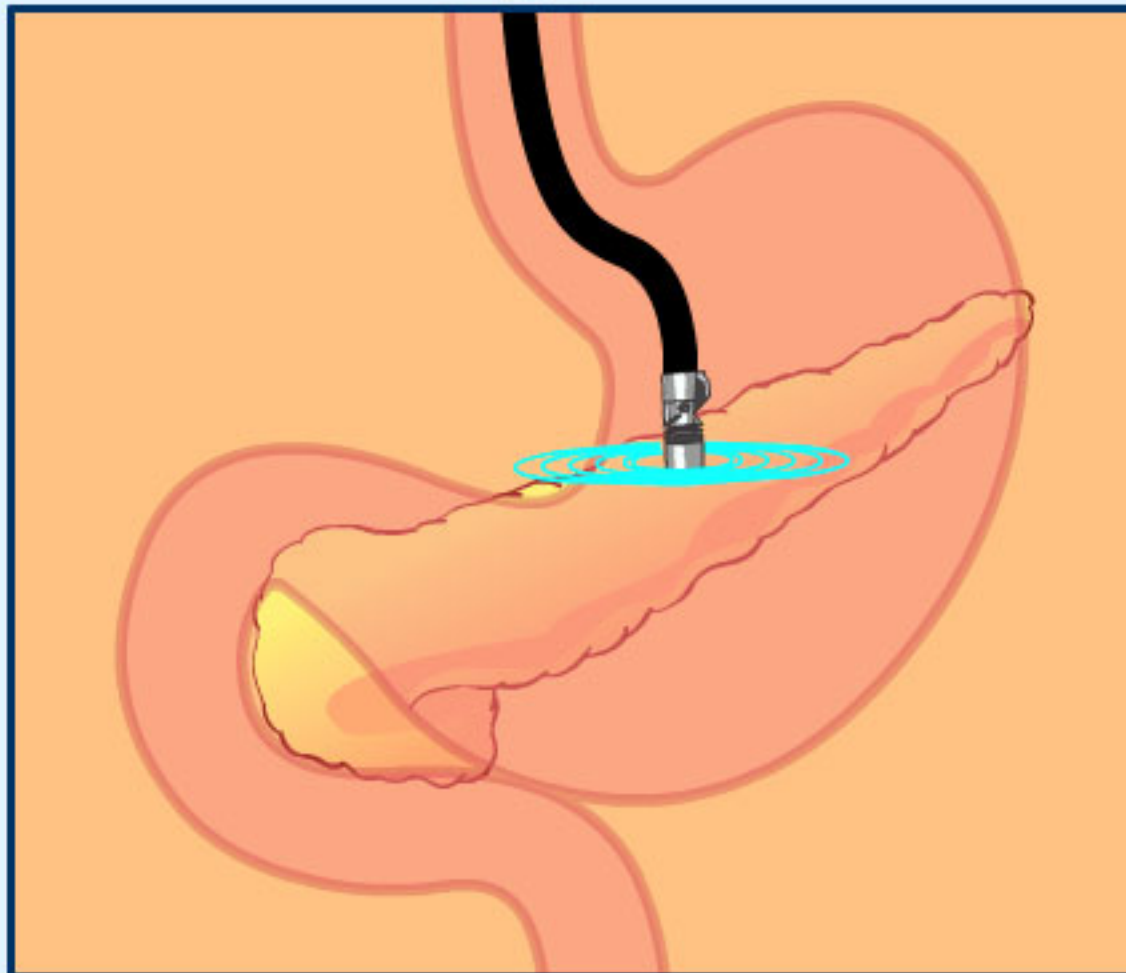
Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Using EUS To Detect Precursor Lesions



EUS involves the insertion of a long tube through the mouth and into the stomach. At the end of this tube is an ultrasound device that can be placed in the part of the stomach that sits closest to the pancreas. This close proximity of the ultrasound device to the pancreas provides very detailed images of the pancreas.

[Start](#)[Pancreas Anatomy](#)[What are Precursor Lesions?](#)[Effects on the Pancreas](#)[EUS Screening](#)[Saving Lives](#)

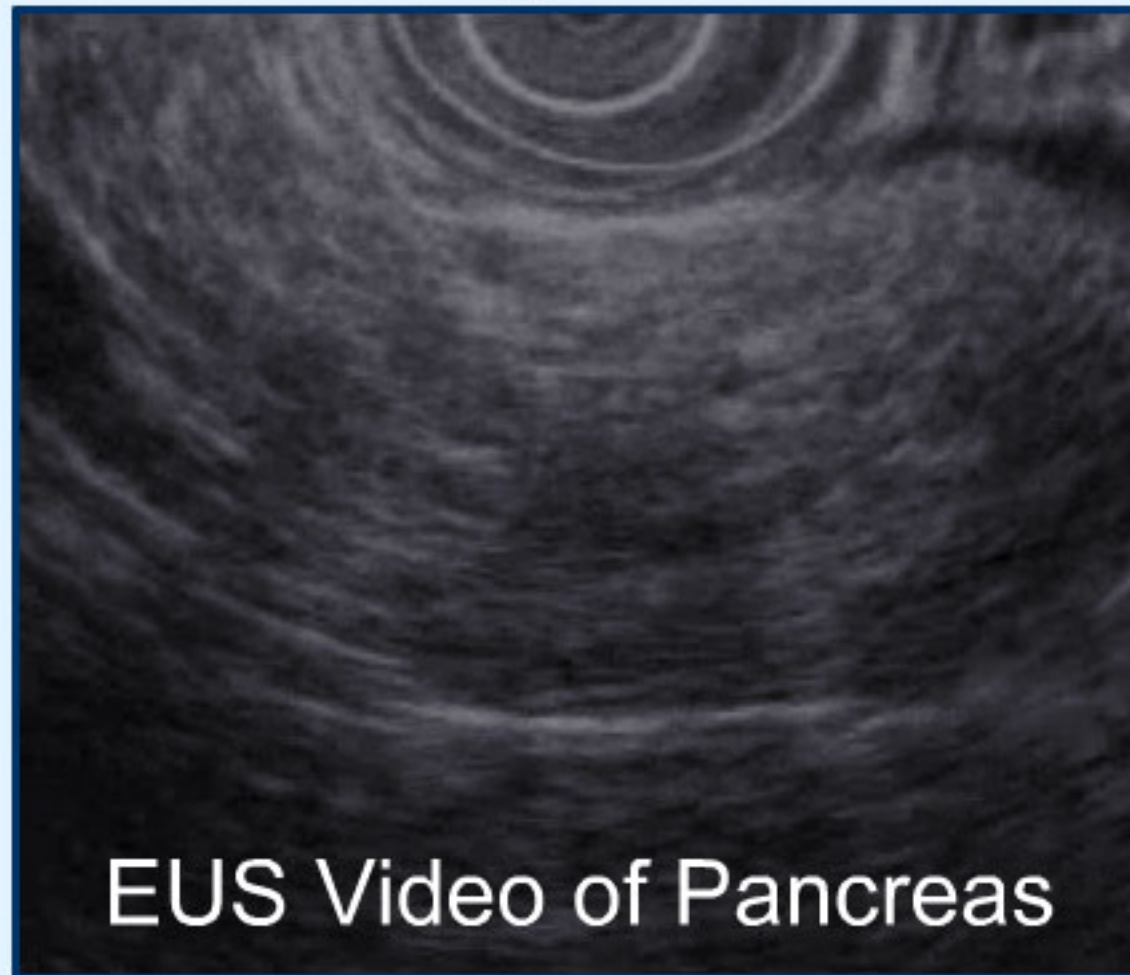
Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Using EUS To Detect Precursor Lesions



At first glance, the images produced by EUS may seem difficult to understand, but a trained ultrasonographer knows what is normal and is able to detect tiny abnormalities.

[Start](#)[Pancreas Anatomy](#)[What are Precursor Lesions?](#)[Effects on the Pancreas](#)[EUS Screening](#)[Saving Lives](#)

Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Using EUS To Detect Precursor Lesions



A healthy pancreas looks like this. Notice the uniform 'salt-and-pepper' appearance.

[Start](#)[Pancreas Anatomy](#)[What are Precursor Lesions?](#)[Effects on the Pancreas](#)[EUS Screening](#)[Saving Lives](#)

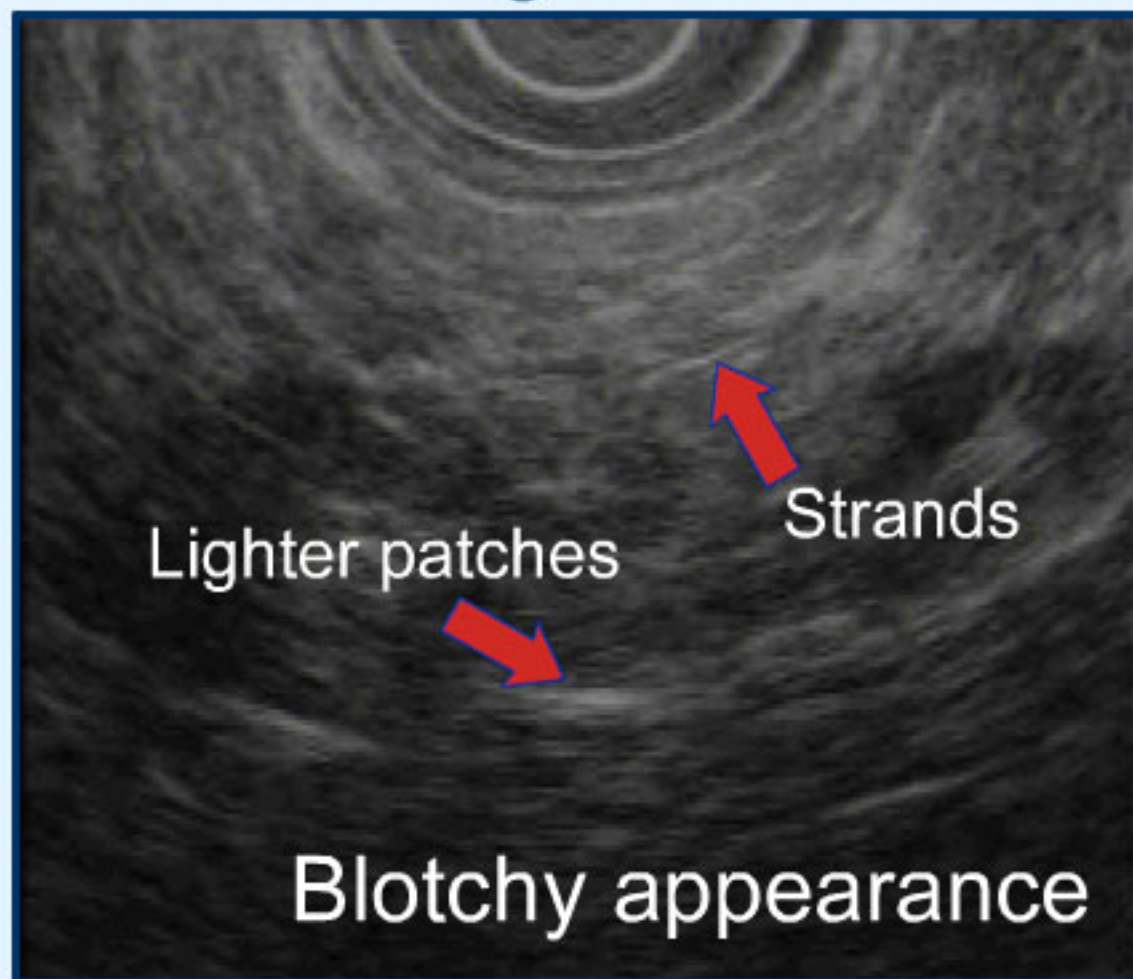
Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Using EUS To Detect Precursor Lesions



A pancreas with PanINs is different. It has a heterogeneous, or blotchy appearance with strands and lighter patches, corresponding to atrophic lobules caused by PanINs.

The PanINs themselves are impossible to make out, but their traces are clearly visible through EUS! Now we have a way to see the precursors to pancreatic cancer before they progress to invasive cancer.



Start

Pancreas
Anatomy

What are
Precursor
Lesions?

Effects
on the
Pancreas

EUS
Screening

Saving
Lives



Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Conclusion: Our Goal is to Save Lives.

**Early Detection
Saves Lives.**

Our goal is to save lives.

Just as mammography screening for breast cancer saves lives and just as colonoscopy for colon polyps saves lives, so too do we want to save lives by detecting and treating precursor lesions in the pancreas **BEFORE** they ever have a chance to progress to pancreatic cancer. The emergent understanding of precursor lesions, as described in this animation, offers great hope for new ways to detect precursor lesions and save lives.



Start

Pancreas
Anatomy

What are
Precursor
Lesions?

Effects
on the
Pancreas

EUS
Screening

Saving
Lives



Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley

Conclusion: Our Goal is to Save Lives.

Hope for the future

Our goal is to save lives.

Just as mammography screening for breast cancer saves lives and just as colonoscopy for colon polyps saves lives, so too do we want to save lives by detecting and treating precursor lesions in the pancreas BEFORE they ever have a chance to progress to pancreatic cancer. The emergent understanding of precursor lesions, as described in this animation, offers great hope for new ways to detect precursor lesions and save lives.

[Start](#)[Pancreas Anatomy](#)[What are Precursor Lesions?](#)[Effects on the Pancreas](#)[EUS Screening](#)[Saving Lives](#)

Audio off



This program is supported by generous educational grants from the Vesalius Trust

© 2006 Johns Hopkins
Created by Lauren O'Malley