INTRODUCTION A LA RECHERCHE EN IMAGERIE

Emmanuel Coche MDPHD
Cliniques Universitaires St-Luc
Avenue Hippocrate,10
1200 Bruxelles
E-mail: Emmanuel.Coche@uclouvain.be
Tél: +3227642918 Fax: +3227705574

Cours 3210

Introduction

- Cibler le sujet/ Etude préliminaire
- Etude préalable de la littérature/biais
- Etude des moyens disponibles
- Statisticien
- Source de financement
- Comité d'éthique
- Se faire aider par des personnes expérimentées: "comité d'encadrement"

Plan Général

- Quelques notions de base
- Comment écrire un article?
- Comment effectuer une présentation?

1. Quelques notions de base

- Sensibilité : vrais + / (vrais + et faux -) : la proportion des patients ayant la maladie qui ont un test positif. Indique la capacité d'un test à identifier une maladie
- Spécificité : vrais - / (vrais - et faux +) : la proportion des patients n'ayant pas la maladie et qui ont un test négatif. Indique la capacité d'un test à identifier les patients sains (non malades)
- Valeur prédictive positive : vrais + / (vrais + et faux +) : la probabilité qu'un patient ayant le test positif ait la maladie
- Valeur prédictive négative : vrais - / (vrais - et faux -) : la probabilité qu'un patient ayant le test négatif n'ait pas la maladie
- Valeurs prédictives dépendent de la fréquence de la maladie dans le groupe étudié

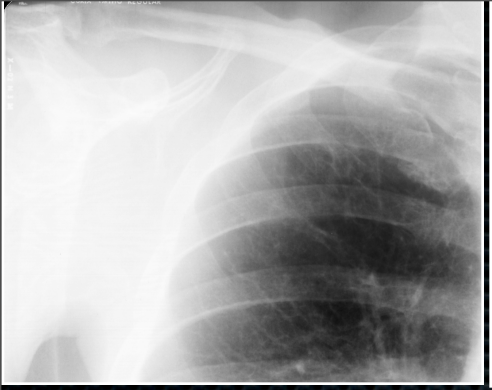
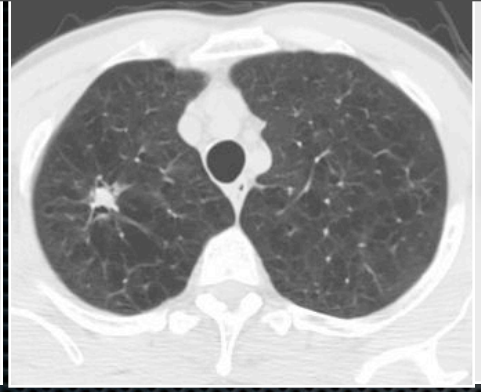
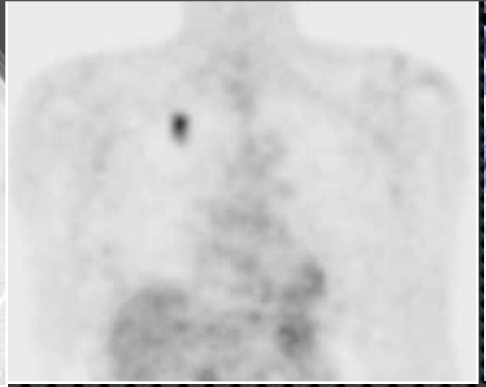
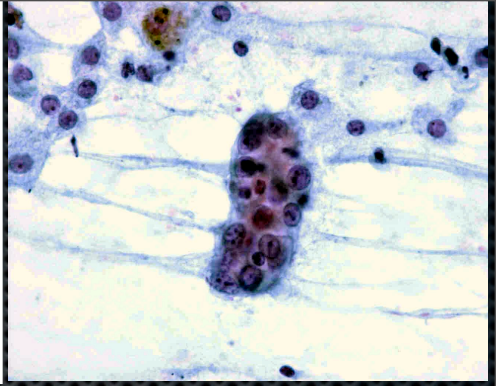
TABLE 1: **Representative of Referral Hospital Population with High Disease Prevalence**

Test		Disease		
		Positive	Negative	Total
Positive	VP	32	FP 1	33
Negative	FN	5	VN 11	16
Total		37	12	49
Prevalence of disease (37/49)				0.76
Sensitivity (32/37)				0.86
Specificity (11/12)				0.92
Positive predictive value (32/33)				0.97
Negative predictive value (11/16)				0.69
Accuracy ([32 + 11]/49)				0.88

TABLE 2: **Representative of Community Hospital with Intermediate Disease Prevalence**

Test	Disease		
	Positive	Negative	Total
Positive	32	10	42
Negative	5	110	115
Total	37	120	157
Prevalence of disease (37/157)			0.24
Sensitivity (32/37)			0.86
Specificity (110/120)			0.92
Positive predictive value (32/42)			0.76
Negative predictive value (110/115)			0.96
Accuracy ([32 + 110]/157)			0.90

Sensibilité : vrais + / (vrais + et faux -)
Spécificité : vrais - / (vrais - et faux +)
Valeur prédictive positive : vrais + / (vrais + et faux +)
Valeur prédictive négative : vrais - / (vrais - et faux -)

Screening for lung cancer

Current guidelines

« At this time, no organization recommend routine screening for lung cancer, either among the general population or in individuals who are at higher risk due to tobacco or occupational exposure »

Smith RA, et al. American Cancer Society guidelines for the early detection of cancer. CA Cancer J Clin (2006);56: 34-49

Introduction

- Lung cancer is
  - The most common cancer in the world
    - 200 10^3 new diagnosed patients in Europe
    - In Belgium: the first cause of cancer in men between 45 and 59 years
  - The leading cause of cancer-related deaths in Europe and in other western countries
    - In Belgium: in 1997: 5,723† in ♂ and 1,090 † in ♀
  - The overall mortality has not changed in decades
    - Five-year survival is 9.6%, ranging from 5.9% in Denmark to 16.2% in Switzerland

Rossi et al. Critical reviews in Oncology and Hematology 2005; 56:311-320 / http://www.registreducancer.org

Distribution of lung cancer

Estimated New Cases*

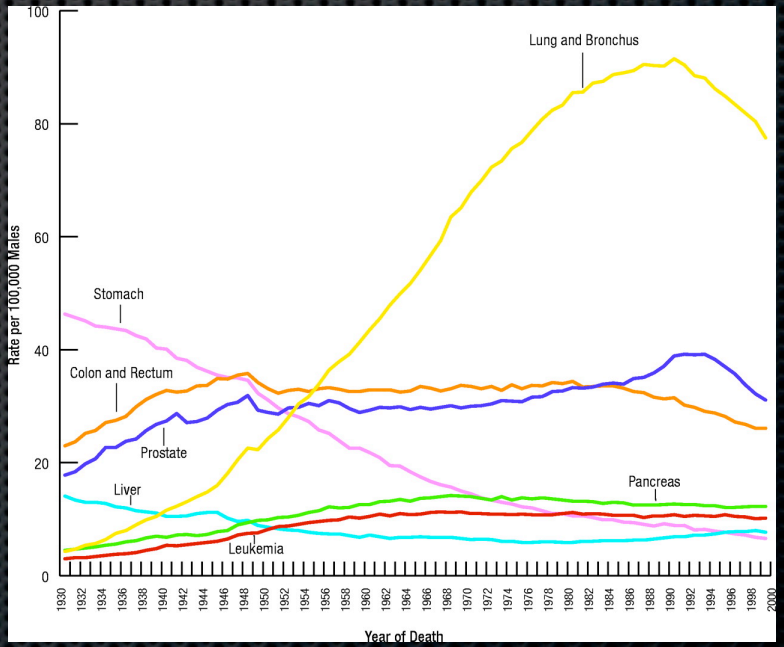
Males			Females		
Prostate	232,090	33%	Breast	211,240	32%
Lung and Bronchus	93,010	13%	Lung and Bronchus	79,560	12%
Colon and Rectum	71,820	10%	Colon and Rectum	73,470	11%
Urinary Bladder	47,010	7%	Uterine Corpus	40,880	6%
Melanoma of the Skin	33,580	5%	Non-Hodgkin Lymphoma	27,320	4%
Non-Hodgkin Lymphoma	29,070	4%	Melanoma of the Skin	26,000	4%
Kidney and Renal Pelvis	22,490	3%	Ovary	22,220	3%
Leukemia	19,640	3%	Thyroid	19,190	3%
Oral Cavity and Pharynx	19,100	3%	Urinary Bladder	16,200	2%
Pancreas	16,100	2%	Pancreas	16,080	2%
All Sites	**710,040**	100%	**All Sites**	**662,870**	**100%**

Estimated Deaths

Males			Females		
Lung and Bronchus	90,490	31%	Lung and Bronchus	73,020	27%
Prostate	30,350	10%	Breast	40,410	15%
Colon and Rectum	28,540	10%	Colon and Rectum	25,750	10%
Pancreas	15,820	5%	Ovary	16,210	6%
Leukemia	12,540	4%	Pancreas	15,980	6%
Esophagus	10,530	4%	Leukemia	10,030	4%
Liver and Intrahepatic Bile Duct	10,330	3%	Non-Hodgkin Lymphoma	9,050	3%
Non-Hodgkin Lymphoma	10,150	3%	Uterine Corpus	7,310	3%
Urinary Bladder	8,970	3%	Multiple Myeloma	5,640	2%
Kidney and Renal Pelvis	8,020	3%	Brain and Other Nervous System	5,480	2%
All Sites	**295,280**	100%	**All Sites**	**275,000**	**100%**

FIGURE 1 Ten Leading Cancer Types for the Estimated New Cancer Cases and Deaths, by Sex, US, 2005.
*Excludes basal and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates are rounded to the nearest 10.
Note: Percentage may not total 100% due to rounding.

American Cancer Society, Surveillance Research, 2005



Population to screen

"The screening test will identify asymptomatic person at risk for a specific disease"

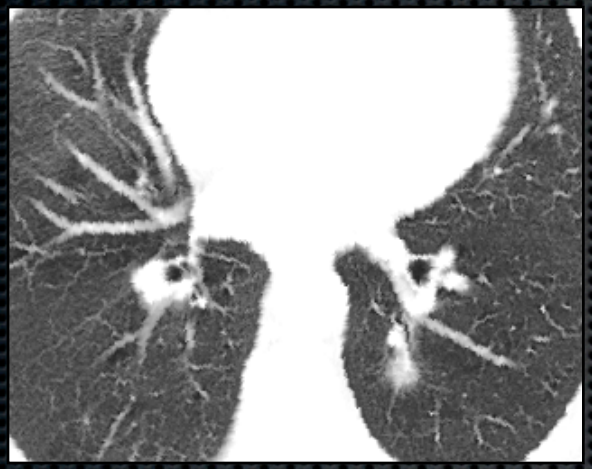
- Subjects between 50 and 80 years old
- Active smokers
- At least 10 pack-years
- High risk population
  - Asbestosis
  - Genetic factors

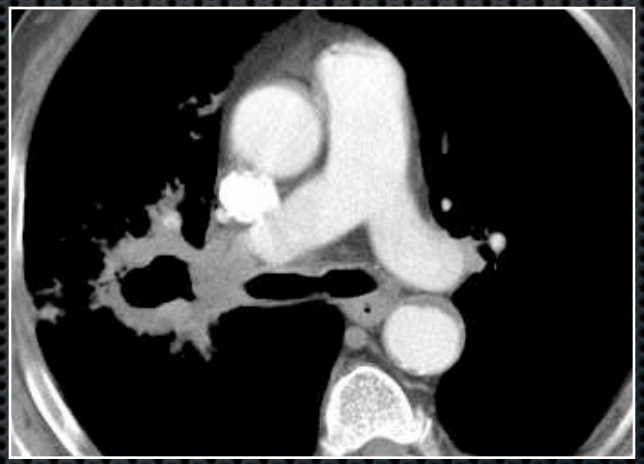
Recommendations of the Society of Thoracic Radiology. Journal of thoracic Imaging 2001;16:65-68

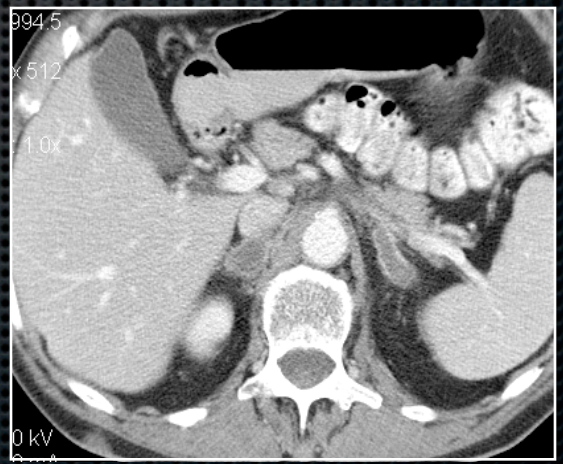
Rationale for lung cancer screening

« Screening is performed to detect disease at a stage when cure or control is possible

Early intervention should change the course of the disease (decreased mortality) »







Stage I

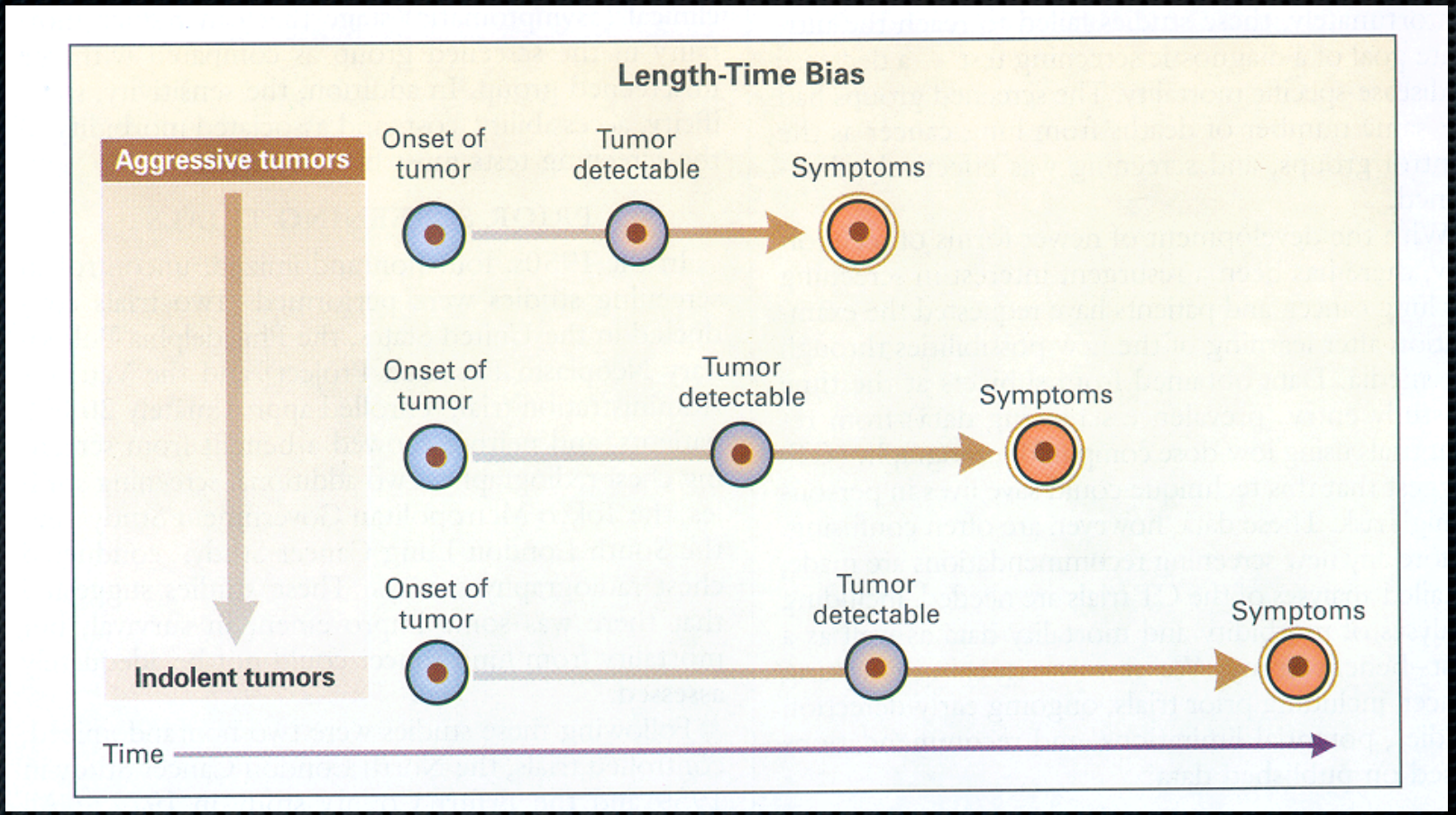
5-year survival after surgery= 70%

Stage IIIa-IV

5-year survival <10%

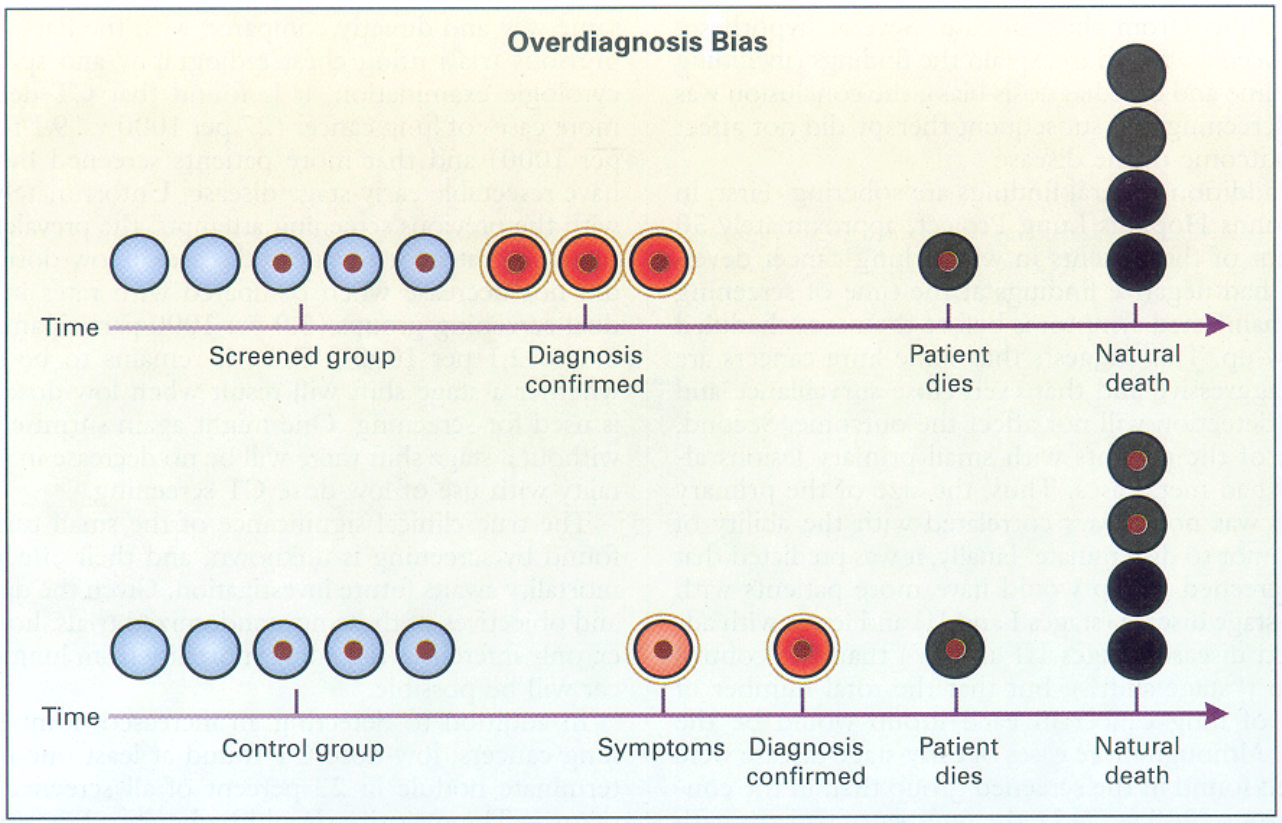
Flehinger BJ et al. The effect of surgical treatment on survival from early lung cancer. Chest 1992;101:1013-1018

Biases in screening



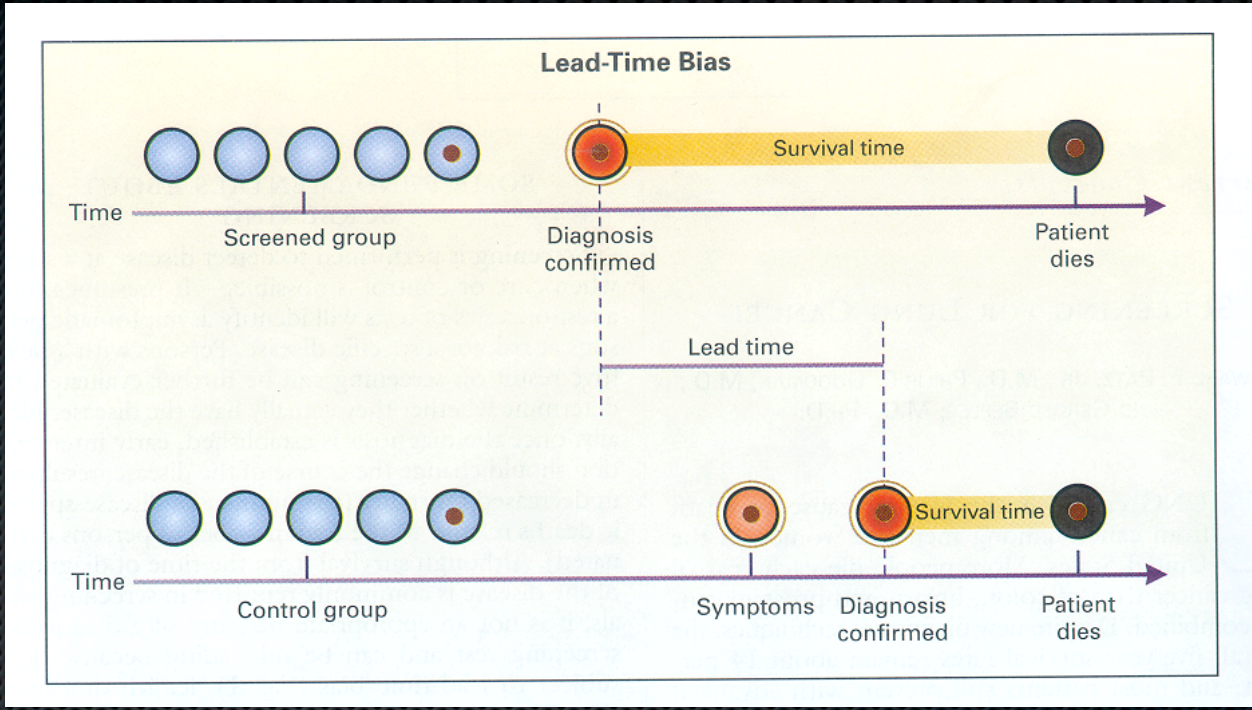
Patz et al. Screening for lung cancer. NEJM 343;22:1627-1633

Biases in screening



Patz et al. Screening for lung cancer. NEJM 343;22:1627-1633

Biases in screening



« Survival from the time of the diagnosis is not an appropriate measure of a diagnostic screening test . Effect of the mortality rather than survival is necessary to validate potential screening methods »

Patz et al. Screening for lung cancer. NEJM 343;22:1627-1633

Imaging in lung cancer screening

«Sensitivity, specificity, accessibility, cost and associated morbidity of the screening test must be reasonable »

Maladies fréquentes

- Pathologies cardiovasculaires
- Cancers
  - Sein
  - Poumon
  - Côlon et rectum

Types d'études

- Etude rétrospective
  - Observations faites à un moment où l'exposition au facteur et maladie ont déjà eu lieu
- Etude prospective
  - débute à un moment où l'exposition au facteur et maladie ont déjà eu lieu
- Etude expérimentale
  - Le chercheur manipule le facteur étudié

Why does single-slice CT not detect sub-segmental PE accurately?

Animal experiments conducted at the Vancouver General Hospital and Jack Bell Research Centre

Vancouver, Canada

Studies supported by the British Columbia Lung Association

1996-1997

Question Nr 1: A problem of vascular distension?

- 7 juvenile domestic pigs
- Anesthesia
- Catheters:
  - Hemodynamic control:
    - Double lumen catheter inserted into the left jugular vein
    - 5F pediatric Swan-Ganz catheter
  - Simulation of injection protocols
    - 18 G catheter introduced into the right brachial vein
    - Catheter into the left jugular vein
    - 6.3 F pigtail catheter placed into the proximal main

Protocols for contrast material administration

Sequence	Site	Injection rate (mL/sec)
1	Peripheral	3.5*
2	Central vein	3.5*
3	Main pulmonary artery	3.5*
4	Peripheral	7.0†
5	Central vein	7.0†
6	Main pulmonary artery	7.0†
7	Main pulmonary artery	20.0‡
8	Main pulmonary artery	40.0**
9	Left pulmonary artery	20.0‡

*Standard rate for peripheral iv injection

† Double rate for peripheral iv injection

‡Standard rate for pulmonary injection

**Double rate for pulmonary injection

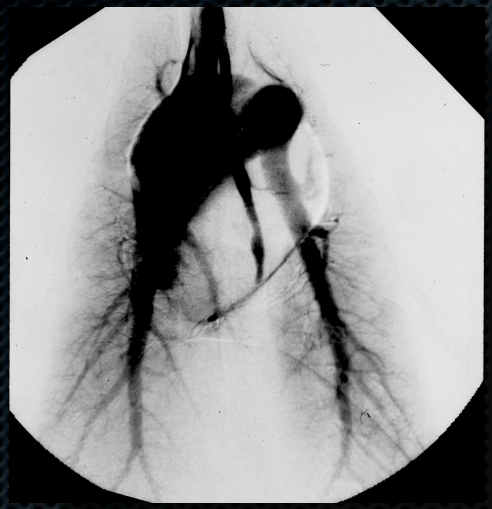
Relationship between vessel size and different sites and different rates of contrast material injection

	Vessel Size (mm)		
Sequence	**Large**	**Medium**	**Small**
1	14.3 ± 1.5 (63)	6.8 ± 1.5 (49)	4.6 ± 0.4 (15)
2	14.6 ± 1.6 (63	6.9 ± 1.3 (34)	4.5 ± 0.4 (12)
3	14.5 ± -0.83 (10)	7.3 ± 1.3 (12)	4.8 ± 0.2 (4)
4	14.6 ± 1.2 (39)	7.4 ± 1.6 (25)	4.5 ± 0.3 (5)
5	14.2 ± 1.4 (63)	7.3 ± 1.5 (40)	4.6 ± 0.4 (25)
6	14.0 ± 1.2 (67)	7.4 ± 1.5 (47)	4.6 ± 0.3 (24)
7	14.1 ± 1.46 (81)	7 ± 1.5 (56)	4.6 ± 0.3 (24)
8	14.6 ± 1.7 (75)	6.8 ± 1.3 (66)	4.5 ± 0.4 (20)
9	14.8 ± 1.4 (77)	7.0 ± 1.5 (86)	4.7 ± 0.3 (13)

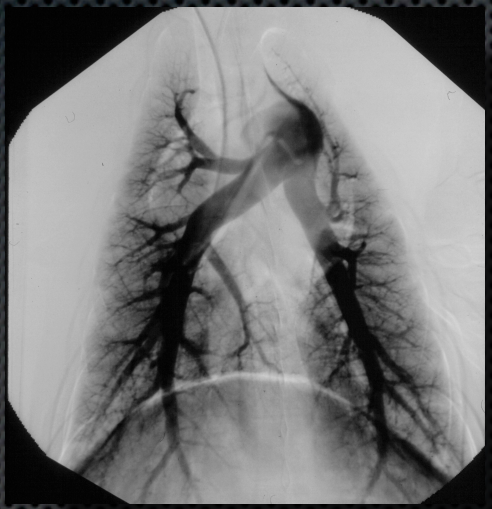
Mean ± standard deviation

ANOVA, $p>0.05$ for all sequences

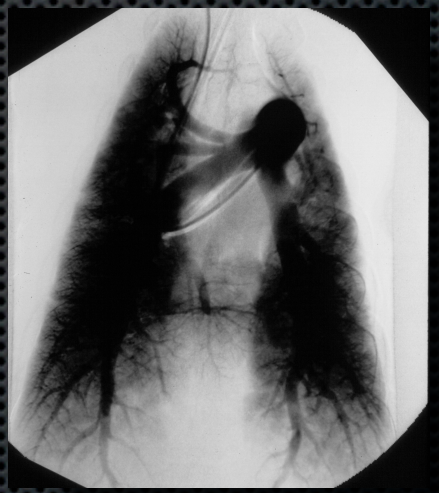
Results



Peripheral intravenous injection



Pulmonary artery injection



Pulmonary artery injection : Q' x 2

The improved detection of subsegmental pulmonary emboli at pulmonary angiography compared with contrast material-enhanced spiral CT **is not due** to differences in vascular distention

Coche E, Baile L, Kim K, Mayo JR.
The effect of contrast injection rate and site on pulmonary vascular distention. Academic Radiology 1999; 6 : 419-425

Question Nr 2: Is pulmonary angiography an appropriate Gold standard?

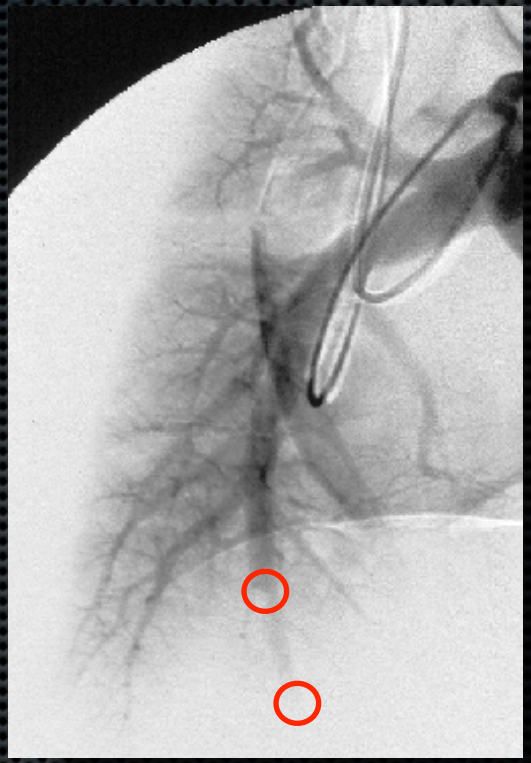
- 16 female juvenile pigs
- Anesthesia + hemodynamic control
- Intravascular catheters: jugular vein, pulmonary artery and right brachial vein
- Artificial emboli (n=86): colored emboli (large: 4.2 mm diameter, green; small: 3.8 mm diameter, red)
- Pulmonary angiography, spiral CT: 1 mm and 3 mm collimation

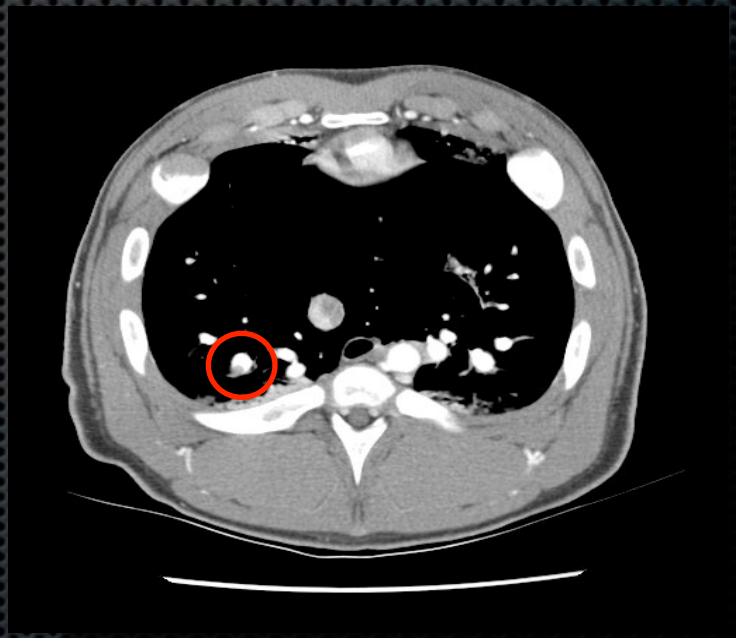
Baile L, King G, Müller N, D'Yachkova Y, Coche E, Pare P, Mayo JR. Spiral computed tomography is comparable to angiography for the diagnosis of pulmonary embolism. Am J Respir Crit Care Med. 2000 Mar;161(3 Pt 1):1010-5.

A new animal model for pulmonary embolism

Anterior view Posterior view

Answer Nr 2: Pulmonary angiography is not an appropriate Gold standard





Baile L, King G, Müller NL, D'Yachkova Y, Coche EE, Pare P, Mayo JRSpiral computed tomography is comparable to angiography for the diagnosis of pulmonary embolism. Am J Respir Crit Care Med. 2000 Mar;161(3 Pt 1):1010-5.

Sensitivity (%) for experimental subsegmental emboli

	CT3	CT1	Angio
Reader 1	89	87	83
Reader 2	74	87	91
Mean	82	87	87
95%CI	73-88	79-93	79-93

No difference between CT and angiography: p= 0.42

No difference between readers

2/Comment écrire un article ?

1/Comment écrire un article scientifique?

Exemple pratique:

Baile EM, King GG, Müller NL, et al. Spiral computed tomography is comparable to angiography for the diagnosis of pulmonary embolism.Am J Respir Crit Care Med. 2000 Mar;161(3 Pt 1):1010

Article scientifique

- C’est un rapport écrit et publié qui décrit des résultats originaux de la recherche
- Soumis à un peer review
  - 2-5 reviewers, de façon anonyme
  - Soumission électronique
- Edité dans un journal scientifique
  - Évalué par un système de cotation: IF
  - http://adminapps.isiknowledge.com/JCR/JCR?PointOfEntry=Home&SID=Y1Dj8mE6991EgmKGbgk

Différents types d'article

- Editorial: Etat de l'art/Débat sur papier publié
- Article originaux: « full paper»
- Article de revue: éducationnel/scientifique
  - Pictorial essay:revue radiologique
- Case report: description d'1 cas unique en diagnostic/traitement/physiopathologie
- Lettre : commentaire sur publication/ communication courte
- Abstracts/proceedings: sociétés scientifiques

Structure d’un article

- 1.Introduction
- 2.Abstract
- 3.Materiel et methodes
- 4.Résultats
- 5.Discussion
- 6.Références

1.Introduction

- Quelle est la question posée?
- Doit être courte
- Poser en termes simples le but de l'article
- Ne doit pas inclure une revue de la littérature
- Qqs références justifiant l'étude actuelle
- Peut-être écrite avant l'étude proprement dite

Introduction

Pulmonary embolism is a commonly encountered clinical problem that is potentially fatal (1). Because this condition has no specific signs or symptoms its diagnosis relies on imaging techniques. Currently, pulmonary angiography is thought to be the most definitive of the techniques used for the diagnosis of pulmonary embolism (2, 3). However, it is not ideal because it is invasive, expensive (4), and has a 6% risk of morbidity and a 0.5% risk of mortality (5). Because of this, results from survey studies have shown that physicians are reluctant to order pulmonary angiography, even when it is appropriate (6).

Contrast-enhanced spiral computed tomography (spiral CT) is a promising new technique for the diagnosis of pulmonary embolism. In comparison to pulmonary angiography it is less invasive, less expensive, and its use may be more acceptable to physicians (7). Results from previous studies show that the sensitivity of spiral CT is approximately 90% for central, lobar, or segmental pulmonary emboli (2, 3, 8–11). However, the ability of spiral CT to detect subsegmental-sized emboli has not been tested.

In many studies spiral CT has been compared with angiography for the diagnosis of pulmonary emboli, but neither has been compared with an independent gold standard (2, 3, 8–11). The use of angiography as the gold standard assumes that angiography is always correct. Any errors in the gold standard will always be reported as errors for the technique being compared. Results from previous clinical studies have shown that when pulmonary angiography was used to detect subsegmental emboli, the agreement between observers was limited (5, 12). Therefore, the aim of the current study is to compare spiral CT to pulmonary angiography for detection of small pulmonary emboli by using a methacrylate cast of the porcine pulmonary vessels as the independent gold standard.

2.Abstract

- Résumé de l'information contenue dans l'article
- 250 mots dans la plupart des revues
  - Description de l'objectif principal
  - Méthodologie utilisée
  - Résultats principaux
  - Conclusions principales

Abstract

The use of spiral computed tomography (CT) for the diagnosis of pulmonary embolism has been compared to angiography, the current gold standard. However, the accuracy of pulmonary angiography has never been evaluated against an independent gold standard. The aim of this study was to compare contrast-enhanced spiral CT to pulmonary angiography for the detection of subsegmental-sized pulmonary emboli by using a methacrylate cast of porcine pulmonary vessels as an independent gold standard. We studied 16 anesthetized, juvenile pigs and injected colored methacrylate beads (3.8 mm, small; 4.2 mm, large) via the jugular vein. After embolization spiral CT (3 mm and 1 mm collimation), and pulmonary angiography were performed. Pigs were killed and the pulmonary arterial tree was cast using methacrylate. Spiral CT and angiography were interpreted independently by two radiologists. Sensitivity and 95% confidence intervals for 3 mm and 1 mm collimation CT and angiography, respectively, were: 82% (73 to 88%), 87% (79 to 93%), 87% (79 to 93%) ($p = 0.42$). Positive predictive values and 95% confidence intervals for 3 mm and 1 mm collimation CT and angiography, respectively, were: 94% (86 to 94%), 81% (73 to 88%), and 88% (80 to 93%). There was no difference between spiral CT and angiography for detection of subsegmental-sized pulmonary emboli. We conclude that spiral CT is comparable to angiography for detection of pulmonary emboli.
Baile EM, King GG, Müller NL, D'yachkova Y, Coche EE, Paré PD, Mayo JR. Spiral computed tomography is comparable to angiography for the diagnosis of pulmonary embolism.

3.Matériel et méthodes

- Méthodes
- Description logique du design de l'étude, des méthodes utilisées et comment les données ont été analysées
- A écrire avant le début de l'étude
- Se faire aider par un collègue expérimenté
- Doit pouvoir être reproduit par le lecteur

3.Matériel et méthodes

- Design: prospective, rétrospective, randomisée
- Etude descriptive: qui, quoi, pourquoi,quand, et où.
- Si question précise à la recherche: énoncer clairement l'hypothèse testée
- Tests statistiques: décrire les tests statistiques utilisés (+ références)
- $p<0.05$
- Computer (type, version software)

3.Matériel et méthodes

- Participants
- Mode de sélection des participants
  - Consécutifs
  - Non consécutifs
- Comité d'éthique/consentement éclairé
- Dosage des médicaments/produits/machines utilisés
  - Nom générique (nom commercial, nom de la firme, endroit de production)

Methods

Surgical Protocol

Sixteen female juvenile pigs (Large White-Landrace Cross) weighing 29 ± 2 kg were studied in the supine position. The study was approved by the University Animal Experimentation Committee and was carried out according to the Candian guidelines for use and care of animals. Anesthesia was induced by intramuscular injection of ketamine hydrochloride (20 mg/kg) (Ketalean; MTC Pharmaceuticals, Cambridge, ON, Canada). The pigs were intubated, and ventilated using a tidal volume of 10 to 12 ml/kg and a rate of approximately 12 breaths/min. Anesthesia was maintained by inhalation of 1 to 2% isoflurane (Abott, Montreal, PQ, Canada). A double-lumen (18-gauge) catheter was introduced into the left internal jugular vein for measurement of central venous pressure and the administration of intravenous fluids and drugs as required. A 14-French (Fr) polyethylene catheter was introduced into the left external jugular vein for later injection of the emboli. The right external and internal jugular veins were isolated for later insertion of a Swan-Ganz catheter (5-Fr), and a Grollman angiographic catheter, respectively. A polyethylene catheter (3 mm interior diameter) was inserted into the left carotid artery for measurement of systemic arterial blood pressure. The right brachial vein was exposed and an 18-gauge catheter inserted to allow later injection of contrast media during spiral CT. To prevent leakage of urine a Foley catheter (5-Fr) was inserted into the bladder through a small suprapubic incision. On completion of the surgery, emboli were injected and the pigs were transferred to the imaging suites of our institution. In eight of the pigs pulmonary angiography was done before spiral CT and in the other eight spiral CT was done first.

Manufacture of emboli. Two sizes of colored emboli were made (large, 4.2 mm diameter, green; small, 3.8 mm diameter, red) using Batson's compound (Polysciences Inc., Warrington, PA), a methacrylate resin. These sized emboli are comparable to those of human subsegmental pulmonary arteries (13). The density of the solid resin is similar to blood and, in the absence of contrast media, emboli manufactured from it cannot be distinguished from blood. A total of 86 emboli were injected, ranging from 3 to 8 per pig. Of these, 40 were 4.2 mm in diameter and 46 were 3.8 mm in diameter.

Experimental Protocol

Pulmonary angiography. Pulmonary angiograms were carried out using commercially available Digital Subtraction Angiography (CAS 2000; Toshiba, Tokyo, Japan), and a 40.6-cm image intensifier. The kilovolts peak (kVp) and millampere-second (mAs) were electronically set to provide an entrance exposure of 300 microRAD (magnification factor approximately 1.2). Pigs were placed supine on the imaging table; the position of the pigs and height of the table did not change during acquisition of the images. Using fluoroscopy, the Swan-Ganz catheter was advanced into the main pulmonary artery for measurement of pulmonary arterial pressure. A 6.3-Fr Grollman angiographic catheter was also advanced into the main pulmonary artery using a catheter guide wire (Seldinger technique). Pancuronium bromide (0.15 mg/kg; Abott) was administered 1 min before the injection of contrast medium. The ventilator was turned off at end-inspiration and pulmonary angiograms were obtained at a rate of 3 to 7.5 frames per second. Images were obtained in the anteroposterior, right anterior oblique (25°), and left anterior oblique (25°) projections. Nonionic contrast medium (Optiray 320; Mallinckrodt Medical, St. Clair, PQ, Canada) was injected through the Grollman catheter using a calibrated volume injector pump (Medrad; Mark V, Pittsburgh, PA). The amount and rate of injection of contrast was calculated, according to the formula used for humans in our institution, and adjusted for the pig's weight (0.57 ml/kg and 0.28 ml/kg/s, respectively). The average rate of injection was 14 ml/s, and the total dose was 28 ml. On completion of pulmonary angiography pulmonary arterial pressure was measured again and the Grollman and Swan-Ganz catheters were withdrawn.

Contrast-enhanced spiral CT. The protocol used for obtaining spiral CT images is similar to the one that is currently used for the clinical diagnosis of pulmonary embolism in our institution. Images were obtained while pigs were in the supine position. Pancuronium bromide (0.15 mg/kg) was administered 1 min before the injection of nonionic contrast medium (Optiray 320) via the brachial vein cannula. The ventilator was turned off at end-inspiration and spiral CT scans were obtained (~ 45 s). Two scans were obtained: first using 3-mm collimation (CT3) and next using 1-mm collimation (CT1). Specifications were: CT3: pitch 2, 320 mA, 1 s rotation time and 120 kVp, preparation delay of 13 ± 3.5 s, contrast volume 72 ± 3 ml/run at a rate of 1.7 ± 0.1 ml/s. CT1: as for CT3, except, preparation delay of 12 ± 2 s. Lungs were scanned from the level of the main pulmonary artery to 2 cm cephalad to the posterior costophrenic angle, using a field of view of 24 cm. After acquisition of the data, overlapping reconstructions were made using the standard algorithm. CT3 scans were reconstructed at 1.5 mm spacing (85 ± 4 sections) and CT1 scans at 0.5 mm spacing (187 ± 9 sections). Images were reviewed on a workstation at mediastinal settings (window 350 Hounsfield units [HU], level 35 HU) and lung settings (window 1,500 HU, level −750 HU).

Corrosion casting. After completing the imaging protocol, pigs were given 4,000 U of heparin, deeply anesthetized and killed by injection of sodium pentobarbital and propylene glycol (Euthanyl; MTC Pharmaceuticals, Cambridge, ON, Canada). Pigs were then transported back to the laboratory. The thorax was opened widely and large-bore (~ 6 mm diameter) catheters were inserted into the left atrial appendage and the main pulmonary artery. The descending aorta was ligated. The pulmonary arteries were then flushed gently with 1,000 ml saline. The lungs were inflated slowly (25 to 30 cm water) and allowed to deflate to approximately 12 cm water positive end-expiratory pressure (PEEP). Batson's (90 ± 10 ml) was injected into the pulmonary vasculature, while the cannula in the left atrial appendage remained open to atmosphere. PEEP was maintained until the cast had completely hardened (approximately 4 h) and the lungs were then carefully removed from the chest. To corrode the tissue surrounding the cast, the lungs were immersed in a solution of supersaturated potassium hydroxide (300 g/L water) for approximately 3 to 4 d. To determine the effectiveness of the cast as an independent gold standard for diagnosing emboli, the number of emboli recovered was calculated as a percentage of the number injected.

Assessment of the radiographic images and pulmonary vascular casts. The angiographic images and CT scans were independently assessed by two radiologists (Reader 1 and Reader 2) who were unaware of experimental sequence, number and size of emboli in each pig. The images were read in random order. The angiograms were reviewed on a workstation using a cine loop. The window width and level were selected by the operator. The spiral CT scans were reviewed at mediastinal and lung window settings on a workstation using a track ball to improve visualization of the branching pattern of the pulmonary vasculature. Each reader recorded the exact vascular location of emboli, using a two-dimensional anatomic drawing of the porcine pulmonary arterial tree.

Data Analysis

The accuracy of the readers' diagnoses for the three imaging modalities (angiography, CT3, and CT1) was verified. This included identification of emboli that were not present (false positive) or their failure to detect emboli that were present (false negative) (Figure 1). Their results were compared with the location of the emboli in the methacrylate cast (Figure 1). The sensitivity of each technique, as interpreted by each reader, for emboli of different sizes, was calculated by the proportion of true-positive identifications. It is impossible to calculate the specificity (percentage of true negatives) because it is not possible to count the total number of unaffected arteries. The positive predictive value of each test, for each size of emboli was calculated. Ninety-five percent confidence intervals for sensitivity and positive predictive values were calculated for each size of emboli. The sensitivity and positive predictive value of angiography and spiral CT were calculated. Differences between angiography and spiral CT were assessed using a two-sided test for equality of proportions (14). To illustrate the effect of using a potentially inaccurate gold standard, the data for spiral CT were also analyzed as if angiography were the gold standard. Significance was accepted when $p < 0.05$.

4.Résultats

- Description générale des résultats principaux
- Pas d'interprêtation ou énoncés demandant des références
  - Mots (description)
  - tableaux (résumé des évidences)
  - illustrations (mettent en avant les points forts)
  - statistiques (supportent les énoncés)

4.Résultats

- Mots
- Description des caractéristiques des participants
- Participants « comparables »
- Présentation des réponses aux questions posées
  - Donner une direction aux résultats
  - Mettre en avant les résultats importants
  - Tables et figures entre parenthèses

4.Résultats

- Tableaux
- Lecteurs évitent le texte
- Directemment aux tableaux/illustrations
- Impact visuel important
- Informatifs
- Faciles à comprendre
- Pas de duplicata de données dans tableaux

Results

Lung Cast

Eighty-four of the 86 emboli injected (98%) were recovered in the lung casts. On two occasions, when two or more emboli impacted in the same vessel, the most distal embolus broke away from the adjacent embolus during corrosion of the lung tissue. Five of the 86 embole were located outside the scanned volume of CT. These emboli were in the upper lobes above the level of the main pulmonary artery. The two emboli lost from the cast as well as the five found outside the scanned volume were not included in the analysis. Thus, there were 79 emboli available for diagnosis for each of the imaging modalities and these were included in the analysis; these emboli consisted of 15 large, 18 small, and 46 emboli that combined at 21 locations (17 pairs, 4 triplets) (Table 1). The combined emboli were 2 to 3 times the length of single emboli, but never wider. The sizes of the vessels in which the emboli were located were 3.8 and 4.2 mm in diameter.

Angiography and Spiral CT

Comparison of the mean sensitivity of the three imaging modalities (Table 1, Figure 1) showed that there was no difference between CT3, CT1, and angiography ($p = 0.42$). There was no difference between readers for accuracy of detection of emboli for CT3 ($p = 0.08$), CT1 ($p = 1.00$), or angiography ($p = 0.39$).

The positive predictive values for Readers 1 and 2, for each modality, are shown in Table 2. There was no difference in positive predictive values between CT3, CT1, and angiography ($p = 0.25$, $p = 0.23$, respectively). The positive predictive value for CT1 was less than that of CT3 ($p = 0.014$) owing to the greater number of false positive for CT1. The total number of false positive and false negatives for the two readers for each imaging modality is shown in Table 3. Also shown, in parenthesis, are the number of false negatives and positives that were in identical locations for both readers.

Angiography as the Gold Standard

The effect of using angiography as the gold standard on the sensitivity, positive predictive value, and number of false positives and negatives is summarized in Tables 4 and 5. In this comparison, the sensitivity and positive predictive value for angiography are, by definition, 100% whereas the sensitivity and the positive predictive value for CT3 and CT1 are lower than they were when compared with the cast.

Hemodynamics

There was no change in systemic or pulmonary arterial pressure.

4.Résultats

- Illustrations
- Présenter des faits qui supportent les résultats (photos, graphes,histogrammes)
- Facilement lisibles
  - Recommandations éditeur (format, annotations…)
- Avec légendes
  - Compréhensibles sans lire le texte
  - Format des données, erreurs standards….

4.Résultats

- Statistiques
- Spécifier le type de statistique
- La taille de l'échantillon (n)
- La signification statistique …..,p<0.05)
- Reprendre les valeurs avec ….,p>0.05
- Déviation standard : moyenne (± dev st)
- Décimales: < exactitude de la mesure

5.Discussion

- Section la plus difficile/être conforme au style du journal
- Message clair
- Plusieurs paragraphes (7-8) en ordre logique
  - 3-4 phrases
  - Ne pas répéter l'introduction
  - Placer les nouveautés à la lumière de la littérature
  - Références qui supportent/contredisent les données de votre recherche. Analyser les divergences

5. Discussion

- Donner une appréciation de vos trouvailles de façon honnête
  - Revue critique des faiblesses de l'étude
  - Biais éventuels
- Implications pratiques
- Conclusions
- Remerciements, Fonds de recherche

The results of this study show that in this animal model, spiral CT is comparable to pulmonary angiography for the detection of pulmonary emboli. The results also illustrate the degree to which using angiography as the gold standard can be misleading. Clinically, detection of pulmonary emboli is a common and important diagnostic problem (1); correct diagnosis leads to appropriate therapy, but false-positive and false-negative results are associated with significant risk for the patient. Although angiography has long been considered to be the most accurate technique available for detecting pulmonary embolism, its diagnostic accuracy has not been previously tested against an independent gold standard. Results from this study show that for emboli that are equivalent in size (3.8 to 4.2 mm) to human subsegmental pulmonary vessels (13), angiography has a sensitivity of only 87% and a positive predictive value of 88%.

Another limitation of angiography is that it has been used less frequently than is clinically indicated because it is invasive and is associated with significant morbidity and occasional mortality (5). By comparison, spiral CT is much less invasive, is associated with fewer complications, is less expensive, and is quicker (2–4). Although our results show that spiral CT is comparable to pulmonary angiography for the detection of pulmonary emboli in this porcine model, a number of caveats concerning experimental design should be considered before the results are applied clinically. These include differences between species that might influence lung anatomy, the use of methacrylate "emboli" rather than thrombi, the ability to ensure apnea throughout the scan, the lack of comparison of CT with selective angiography and magnification, and the per embolus rather than per pig analysis.

The pulmonary vascular tree of the pig is not identical to that of humans; there is one large main pulmonary arterial trunk with many smaller vessels as opposed to the more dichotomous branching structure of the human pulmonary vascular tree. However, our emboli were made so that they would lodge in branches of the major trunk which are the same size (3.8 to 4.2 mm) as human subsegmental pulmonary arteries (14). Because there is no reason that the differences in anatomy between pigs and humans should favor improved accuracy of one technique in one species, we do not think that this difference in anatomy influences our major conclusions. The behavior of methacrylate "emboli" could be different from naturally occurring thrombi; specifically the manufactured "emboli" are more rigid than freshly formed clot and therefore might conform less well to the shape of the vessels in which they lodged. If the methacrylate emboli did not completely interrupt blood flow through the vessels in which they lodged then they might be easier to identify using CT rather than angiography. This is because when using CT the diagnosis is based on the identification of the actual embolic material whereas when using angiography the presence of a distal perfusion defect also aids in the identification of emboli.

In this study the image quality was optimized by maintaining apnea throughout the acquisition of the image. This is often not possible to do when patients are dyspneic, especially when obtaining CT images because image acquisition takes considerably longer than angiography. In our study the average time to obtain CT1 and CT3 images was 28 ± 2 and 22 ± 1.4 s, respectively, whereas the average time for angiography was less than 10 s. Although respiratory motion would affect interpretation of both CT and angiography, the longer time for CT image acquisition could mean that these images would be more difficult to interpret. This potential problem will be minimized with the advent of multidetector CT which will shorten the acquisition time.

In this study angiography was performed only after main pulmonary artery injection of contrast material. Current techniques for obtaining pulmonary angiographic images for detection of emboli in humans often involve selective angiography and occasionally magnification techniques which may improve the results of angiography. However, we performed angiography with frontal and two oblique projections and used a reduced field of view because of the small size of the pigs. Thus we do not think that this was a major factor in decreasing the sensitivity of angiography.

To compare the accuracy of techniques to detect pulmonary emboli, an analysis by subject rather than, or in addition to, by embolus would be desirable. The decision to treat or not to treat a patient for pulmonary emboli is based on deciding whether the patient has *any* pulmonary emboli rather than how many. However, our study design was not intended for such a comparison. In fact, all of the techniques detected at least one embolus in each pig so that, on a per pig basis, both techniques were 100% sensitive. We have calculated that in order to do a per pig study in which an appropriate number of unaffected pigs were included and which had sufficient power to detect an approximately 10% difference in accuracy between the techniques, we would have had to study more than 200 pigs. Therefore, we have adopted a per embolus experimental design for pragmatic reasons.

Although CT1 was more sensitive than CT3, its positive predictive value was less than CT3 or angiography owing to a greater prevalence of false positives. This was partly attributable to the decrease in the concentration of contrast media within the pulmonary vasculature on the most caudal sections of the lung as a consequence of the longer acquisition time required to obtain images at 1-mm collimation. It is possible that a more prolonged infusion of radiocontrast media, and/or a faster imaging time, as will soon be possible with the advent of multirow detector scanners, will make CT1 more accurate than CT3 or angiography.

The results of this study illustrate the difficulty of assessing a new diagnostic technique when the accepted gold standard is less than perfect. Comparison of angiography to the vascular cast clearly demonstrated that angiography had both false-positive and false-negative diagnoses. Spiral CT, or any other modality that is being compared with an inaccurate gold standard, will inevitably be penalized. For example, if angiography is used as the gold standard then no false positive or negatives can be attributed to it. In this study angiography failed to detect eight emboli that were correctly identified by CT3 and eight emboli that were correctly identified by CT1, and these were assigned as false positives for spiral CT (38% of all the false positives attributed to CT3 and CT1). Similarly, angiography detected 12 false-positive interpretations of pulmonary emboli that were (correctly) not diagnosed by CT3 and 12 that were (correctly) not diagnosed by CT1. These were assigned as false negatives for spiral CT (52% of all the false negatives attributed to CT3 and CT1). Only by comparing both diagnostic techniques with a true gold standard were we able to demonstrate that spiral CT and angiography were comparable for detecting subsegmental-sized emboli.

This study has limitations that are intrinsic to the experimental design. Spherical emboli manufactured from Batson's compound can only approximate the fragmented clot found in clinical pulmonary embolism. The size and branching pattern of the pulmonary vasculature of the pig is substantially different from that of humans (15), and the readers' lack of experience with this branching pattern may have contributed to the high rate of false positives on interpreting the CT1 images. A longer "breath-hold" time was required to acquire the tomographic images (CT3, 22 ± 1.4 s; CT1, 28 ± 2 s) than the angiographic images (< 10 s). In a clinical setting a dyspneic patient may not be able to hold their breath for as long as this, and consequently, the accuracy of spiral CT could be affected. The introduction of multidetector scanners will minimize this potential limitation.

Conclusion

In conclusion, results from this study demonstrate that angiography and spiral CT are comparable for the detection of pulmonary emboli. These results support the use of spiral CT as a primary diagnostic modality in suspected pulmonary embolism, and as the diagnostic tests of choice when ventilation–perfusion scans are judged to be intermediate probability. However, if poor image quality is obtained as a result of motion artifacts while using spiral CT, then pulmonary angiography should be considered.

6.Références

- Procurent le «background» scientifique
- Recherche de litérature et lecture doivent se faire avant tout projet de recherche
- Recherche de litérature: pubmed
  - http://www.ncbi.nlm.nih.gov/pubmed/
- Reference manager
- Style en fonction du journal

Références

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Tables

TABLE 1

SENSITIVITY (%) FOR DETECTING PULMONARY EMBOLI USING SPIRAL CT AND ANGIOGRAPHY

	CT3 mm Collimation				CT1 mm Collimation				Angiography			
Size	Large	Small	Comb	Overall Mean	Large	Small	Comb	Overall Mean	Large	Small	Comb	Overall Mean
Emboli in cast*	15	18	21		15	18	21		15	18	21	
Reader 1	93	78	95	89	100	67	95	87	80	67	100	83
Reader 2	80	44	95	74	93	67	100	87	87	83	100	91
Mean: R1, R2	87	61	95	82	97	67	98	87	83	75	100	87
95% CI				73–88				79–93				79–93

Definition of abbreviations: 95% CI = 95% confidence interval; R1 = Reader 1; R2 = Reader 2.
* Number of emboli in the cast that were used in the analysis (*see* text).

TABLE 2

POSITIVE PREDICTIVE VALUES (%) FOR DETECTION OF PULMONARY EMBOLI

	CT3 mm	CT1 mm	Angiography
Reader 1	96	81	87
Reader 2	91	81	89
Mean: R1, R2	94	81	88
95% CI	86–94	73–88	80–93

TABLE 3

TOTAL NUMBER OF FALSE POSITIVES AND NEGATIVES IDENTIFIED BY THE TWO READERS*

	CT3 mm	CT1 mm	Angiography
False negatives	20 (4)	14 (4)	14 (4)
False positives	6 (1)	22 (2)	13 (2)

* The number of false negatives or positives that were identical for both readers is shown in parentheses.

TABLE 4

ANGIOGRAPHY AS THE GOLD STANDARD: SENSITIVITY (%)

	CT3 mm	CT1 mm	Angiography
Reader 1	79	79	100
Reader 2	73	84	100
Mean: R1, R2	76	81	100

TABLE 5

ANGIOGRAPHY AS THE GOLD STANDARD: POSITIVE PREDICTIVE VALUE (%)

	CT3 mm	CT1 mm	Angiography
Reader 1	82	71	100
Reader 2	91	79	100
Mean: R1, R2	86	75	100

Qqs conseils

- Ecrire l'article avant que la recherche ne se termine
- Le titre et l'abstract peuvent être écrits en dernier lieu
- L'autorship doit être décidé à l'avance
- Si l'article est refusé, le resoumettre avec modifications
- Faire relire l'article par un médecin anglophone en fct de la revue

Qqs conseils

- Bien cibler le journal
- Vaut mieux parfois envoyer dans un journal général que dans un journal de spécialité
- Ne pas se décourager !
- Se faire conseiller !
- Ecrire est un métier !

2/Comment faire une présentation orale?

“Ce qui se conçoit aisément s’énonce clairement”

Logiciels disponibles

- Power point (microsoft office)
  - le plus répandu
  - Utilisé dans les congrès avec lecture centralisée
  - Facile d'utilisation
- Keynote (Apple)
  - + créatif
  - + restrictif
  - transformation en différents fichiers
  - exportable en ppt

Règles générales

- Contenu
  - Clair
  - Structuré
  - Léger
  - Synthétique
- 2 diapositives/minute
- Pas d ’éléments distracteurs

Fonds de diapositive

- Fond sobre
- Eviter les couleurs flash
- Fond bien distinct du lettrage et annotations
- Garder le même masque de diapositive
  - Interchangeabilité

Structure

- I Titre
- II Introduction
  - Hypothèse-justification-litterature-objectifs
- III Méthodes
  - Equipement-échantillonage-méthodes d'analyse
- IV Résultats et discussion
  - Objectifs accomplis/Données
- V Conclusions

Police

- Eviter polices trop petites
- Couleurs contrastées
- Eviter lettres capitales
- Phrases doivent remplir l'espace diapo (interligne)
- Italique ou gras pour mettre en évidence

Images

- Images assez grandes
- Fond sombre
- Eléments graphiques (flèches)
- Illustration des propos tenus
- En nombre raisonnable

Tableaux

- Strict minimum
- Nombre de colonnes et lignes
- Couleur des polices et fonds
- Taille des caractères: lisible
- Mettre en évidence les données les plus relevantes

Animations

- Permettent d’attirer l’attention de l’audience
- Ne pas en abuser
- Eviter les “sons”
- Transitions permettent de passer d’un sujet à l’autre

Lectures conseillées

- How to write a paper. 3rd edition. Edited by George M Hall. BMJ books, 2003,London WC1H9JR
- Wow to write and publish a scientific paper. Robert A Day.Isi press,1979, Philadelphia, Pennsylvania 19104