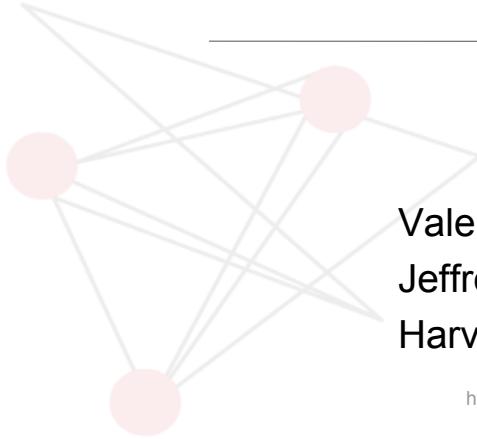




THE HARVARD CLINICAL  
AND TRANSLATIONAL  
SCIENCE CENTER

# Benefits and Risks of Imaging

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<http://catalyst.harvard.edu>



## Outline

- **Harvard Catalyst Imaging Consortium**
- **Benefits and Risks of Imaging**
- **References**

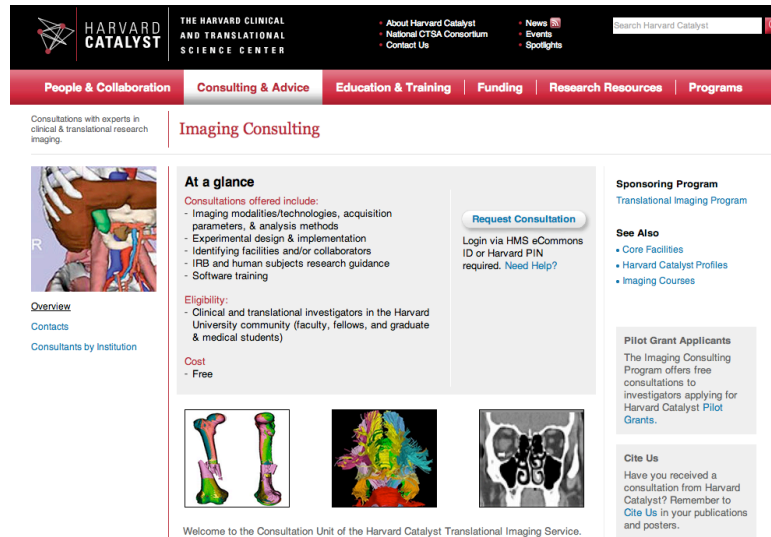
## Harvard Catalyst Imaging Consortium

- **Provide expert consultation and guidance to the CTSC participants in the use of imaging as part of clinical translational research**
- **Educate and advise about available imaging and image processing capabilities in the Harvard environment**

## Harvard Catalyst Imaging Consortium

 <p><b>MASSACHUSETTS GENERAL HOSPITAL</b></p>	<p><b>Bruce Rosen, Director</b> <b>Randy Gollub, Co-Director</b> <b>Gordon J. Harris, Consultant</b> <b>William Hanlon, Consultant</b></p>
 <p><b>Beth Israel Deaconess Medical Center</b></p>	<p><b>Robert Lenkinski, Consultant</b> <b>Ivan Pedrosa, Consultant</b></p>
 <p><b>BRIGHAM AND WOMEN'S HOSPITAL</b> <small>A Teaching Affiliate of Harvard Medical School</small></p>	<p><b>Clare Tempany, Consultant</b> <b>Ron Kikinis, Consultant</b> <b>Charles Guttman, Consultant</b> <b>Todd Perlstein, Consultant</b> <b>Gordon Williams, PI for CTSC Translational Technologies</b></p>
 <p><b>Children's Hospital Boston</b> <small>The Hospital for Children</small></p>	<p><b>Stephan Voss, Consultant</b> <b>Simon Warfield, Consultant</b></p>
 <p><b>DANA-FARBER CANCER INSTITUTE</b></p>	<p><b>Annick D. Van den Abbeele, Consultant</b> <b>Jeffrey Yap, Consultant, Director of Education</b></p>
 <p><b>HARVARD CATALYST</b> THE HARVARD CLINICAL AND TRANSLATIONAL SCIENCE CENTER</p>	<p><b>Valerie Humblet, Imaging Liaison</b> <b>Yong Gao, Imaging Informatics Architect</b></p>

<http://catalyst.harvard.edu/services/imagingconsult/>



The screenshot shows the Harvard Catalyst website's 'Imaging Consulting' page. The header includes the Harvard Catalyst logo and navigation links: 'People & Collaboration', 'Consulting & Advice', 'Education & Training', 'Funding', 'Research Resources', and 'Programs'. The main content area is titled 'Imaging Consulting' and features a 'Request Consultation' button. Below this, there are sections for 'At a glance' (listing services like imaging modalities, experimental design, and software training), 'Eligibility' (clinical and translational investigators), 'Cost' (free), 'Sponsoring Program' (Translational Imaging Program), 'See Also' (Core Facilities, Harvard Catalyst Profiles, Imaging Courses), 'Pilot Grant Applicants' (free consultations for pilot grants), and 'Cite Us' (instructions for citing the service). The page also includes several medical images: a 3D anatomical model of a hand, two 3D models of bones, a 3D model of a brain, and a CT scan of a chest.

## Objectives

- **Understand the benefits and risks of x-ray, CT, MRI, PET, and ultrasound**
- **Learn the risks of imaging contrast materials used in CT, MRI, and ultrasound**
- **Understand the potential risks of ionizing radiation used in imaging**

## Benefits versus Risks

- **We must focus on knowing/reducing the risks. Benefits should always outweigh the risks**

### Risks

Claustrophobia  
Discomfort  
Noise  
Radiation Exposure  
Contrast reactions



### Benefits

Non-invasive  
Early detection  
Staging  
Response assessment  
Pharmacokinetics  
Pharmacodynamics  
Biopsy/Surgical guidance  
Safety monitoring

## Benefits of Imaging

- **Detection and diagnosis of disease at its earliest, most treatable stages**
- **Staging (spread of disease)**
- **Re-staging (evaluation at end of treatment)**
- **Monitoring therapy (early or intermediate response assessment)**
- **Image-guided planning (surgery, radiation therapy)**
- **Not only improve health outcomes and save lives, but also reduce health care costs**

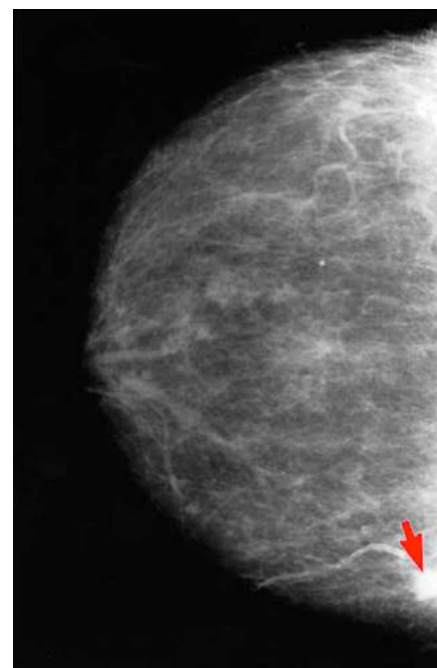
## Benefits examples

- **For all cancers, PET scanning allowed to avoid additional tests or procedures 77% of the time. In 36% of cases, it resulted in a physician's decision to alter the patient's course of treatment**
- **Coronary Computed Tomographic Angiography (CCTA) rules out coronary artery disease with over 90% accuracy, saving patients from unnecessary surgery**

<http://www.medicalimaging.org/>

## Mammography

- **Uses a low-dose X-ray system to examine breasts**
- **Used to aid in the early detection and diagnosis of breast diseases in women**
- **Only used for detecting locoregional disease (not a whole-body technique)**



## Mammography

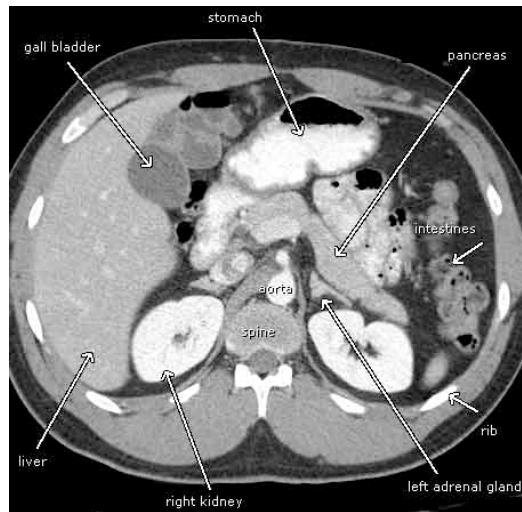
- **Benefits**
  - **Very low radiation dose procedure. X-rays usually have no side effects in the diagnostic range**
  - **High spatial resolution capable of detecting small lesions**

## Mammography

- **Risks**
  - **Always a slight chance of cancer from excessive exposure to radiation**
  - **False Positive: 5 to 15% of screening mammograms require more testing ultimately confirming that no cancer was present (example: deodorant, talcum powder or lotion under arms or on breasts can appear as calcium spots)**

## Computed Tomography (CT)

- **Combines special x-ray equipment with sophisticated computers to produce 3D whole body imaging**
- **Images of internal organs, bones, soft tissue and blood vessels**



## Computed Tomography (CT)

- **Ideal for image guidance: biopsy, surgery, radiation**
- **Standard for response assessment in trials**
- **Diagnoses problems such as cancers, cardiovascular disease, infectious disease, appendicitis, trauma and musculoskeletal disorders**

## **Computed Tomography (CT) Benefits**

- **Painless, noninvasive and accurate**
- **Ability to image bone, soft tissue and blood vessels all at the same time**
- **Very detailed images**
- **Fast and simple; in emergency cases, they can reveal internal injuries and bleeding quickly enough to help save lives**
- **Less sensitive to patient movement than MRI**
- **Can be performed on people with implanted medical device, unlike MRI**

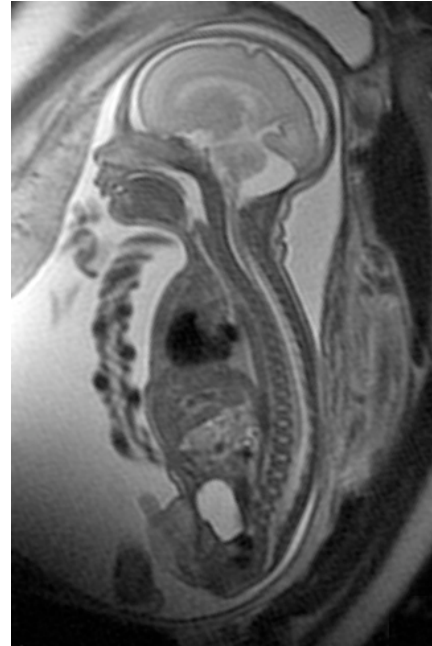
## **Computed Tomography (CT) Risks**

- **Higher radiation dose than planar X-ray**
- **Not recommended for pregnant women (potential risk to the baby)**
- **Nursing mothers should wait for 24 hours after contrast material injection before breast-feeding**
- **Rare risk of serious allergic reaction to contrast materials that contain iodine**
- **Children: CT study only if it is essential for making a diagnosis and should not have repeated CT studies unless absolutely necessary**



## Magnetic Resonance Imaging (MRI)

- **Noninvasive, high resolution 3D imaging modality**
- **Uses a powerful magnetic field, radio frequency pulses and a computer to produce detailed pictures of organs, soft tissues, bone and virtually all other internal body structures**



Compendium of fetal MRI, D. Levine

## Magnetic Resonance Imaging (MRI) Benefits

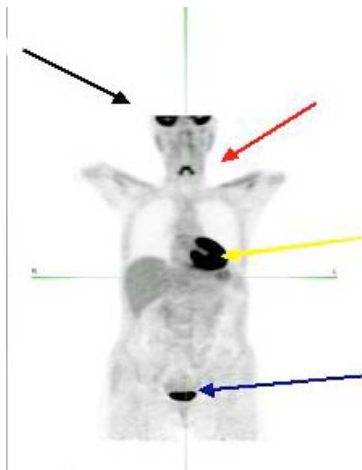
- **No exposure to ionizing radiation**
- **Proven valuable in diagnosing cancer, heart and vascular disease and muscular and bone abnormalities**
- **Enables discovery of abnormalities that might be obscured by bone with other imaging methods**
- **The contrast material is less likely to produce an allergic reaction than the iodine-based contrast materials used for conventional X-rays and CT scanning**

## Magnetic Resonance Imaging (MRI) Risks

- **Not acceptable for some patients: implanted metallic medical devices may malfunction or cause problems**
- **Very slight risk of an allergic reaction to contrast material**
- **Nephrogenic systemic fibrosis**
- **Noise, claustrophobia**

## Positron Emission Tomography (PET)

- **Nuclear medicine imaging**
- **Functional and molecular imaging modality**
- **Diagnoses many types of cancers, heart disease and certain other abnormalities within the body**
- **Uses radioactive material that accumulates in certain area of the body, where it gives off energy in the form of gamma rays**



## Positron Emission Tomography (PET) Benefits

- **Provides unique information: can measure cellular-level metabolic changes**
- **Can detect diseases at their earliest stages, since disease processes often begin with functional changes at the cellular level**
- **Nuclear medicine is less expensive and may yield more precise information than exploratory surgery**

## Positron Emission Tomography (PET) Risks

- **Exposition to radioactive material, but in very low doses that do not affect normal bodily functions**
- **Injection of the radiotracer may cause slight pain and redness**
- **Pregnant or breastfeeding women should discuss the risks and benefits with their doctors before having the tests performed**

## PET/CT

- **Provides images that pinpoint the location of abnormal metabolic activity within the body**
- **Higher level of accuracy; reduces differences in patient positioning**
- **Greater convenience for the patient who undergoes two exams at one sitting**



## Ultrasound

- **Uses high-frequency sound waves**
- **No ionizing radiation**
- **Real-time image capture, show structure and movement, as well as blood flow**
- **Not a whole-body technique**
- **Useful for biopsy guidance**



## **Contrast Enhanced Ultrasound**

- **Use of microbubbles (targeted or untargeted) that reflect the US waves.**
- **Applications:**
  - **Organ Edge Delineation**
  - **Blood Volume and Perfusion:**
  - **Inflammation (Crohn's disease, atherosclerosis)**
  - **Cancer (angiogenesis)**

## **Ultrasound Benefits**

- **Noninvasive and usually painless**
- **Widely available, easy-to-use and less expensive than other imaging methods**
- **No ionizing radiation**
- **Gives a clear picture of soft tissues that do not show up well on X-ray images**
- **Preferred imaging modality for the diagnosis and monitoring of pregnant women and their unborn babies**

## **Ultrasound Risks**

- **For standard diagnostic ultrasound there are no known harmful effects on humans**
- **Risks linked to contrast agents discussed later**

## **Contrast Agents**

- **Used in CT, MRI, and ultrasound**
- **Enhance the difference in image intensity between the object of interest (e.g. tumor) and background tissue**
- **Can be administered intravenous or orally**
- **Compounds are treated as drugs and require adequate safety procedures**

## General risks of injection

- **Irritation**
- **Infection at site of injection**
- **Extravasation (0.1%-0.9%)**
- **Air embolism**

## Risks of iodinated Contrast Agents

- **Iodinated contrast media are frequently used and are safe**
- **Reactions, when they occur, are usually mild but may occasionally progress to life-threatening proportions**
- **A thorough understanding of the etiology, predisposing factors, symptoms, and management strategies is effective in minimizing the threat posed by these factors**

## **Risks of iodinated Contrast Agents**

- **Anaphylactoid/Idiosyncratic reactions**
  - **Mild: skin rash, itching, nasal discharge, nausea, and vomiting**
  - **Moderate: persistence of mild symptoms, facial or laryngeal edema, bronchospasm, dyspnea, tachycardia, or bradycardia**
  - **Severe: life- threatening arrhythmias, hypotension, overt bronchospasm, laryngeal edema, pulmonary edema, seizure, syncope, and death**

J Nucl Med Technol 2008; 36:69-74

## **Risks of iodinated Contrast Agents**

- **Nonanaphylactoid reactions**
  - **Cardiovascular, respiratory, urinary, gastrointestinal, and nervous systems are most commonly affected by physiologic changes produced by contrast media.**
  - **The symptoms of nonanaphylactoid reactions are warmth, metallic taste, nausea, vomiting, bradycardia, hypotension, vasovagal reactions, neuropathy, and delayed reactions**

J Nucl Med Technol 2008; 36:69-74



## **Risks of iodinated Contrast Agents**

- **Delayed Reactions: 1 hr-7 days after injection (approximately 2% of patients)**
  - **Common flu-like symptoms (fever, chills, rashes, pruritus, and nausea).**
  - **Less-frequent manifestations are parotitis, joint pain, and depression.**
- **Contrast-Induced Nephrotoxicity**
  - **Estimated incidence of 2-7%**
  - **Multiple risk factors (e.g. renal disease)**
  - **Requires thorough screening**

J Nucl Med Technol 2008; 36:69-74

## **Ultrasound contrast: microbubbles**

- **FDA approved agent used in cardiology (Lantheus: Definium)**
- **Active clinical trials in U.S. to evaluate agent currently used clinically in Europe (Bracco: Sonovue)**
- **Previous FDA black box restriction for cardiac incidents**

## Ultrasound contrast: microbubbles

- **Sonovue safety profile/risk**
  - Headache, warmth, flushing
  - Nausea, chills, chest pain
- **5 deaths/2 million doses = 1/400,000**
  - Echocardiographic (unstable angina): 3
  - 9 hour post contrast: 1
  - Anaphylactoid reaction: 1
- **MRI/CT death: 1-3/100,000 (0.002%)**

## Risks of MRI contrast agents

- **Most commonly used contrast agents are gadolinium-based**
- **Anaphylactic reactions are rare but do occur**
- **Nephrogenic systemic fibrosis (NSF):**
  - **Newly discovered disease (1997) associated with the use of Gd-based MRI contrast agents in patients with severe renal disease disorder**
  - **Characterized by thickening and hardening of the skin and immobility or tightening of the joints**
  - **Screening for risk factors for kidney disease (> 60 years, diabetes, systemic lupus erythematosus, history of renal disease, multiple myeloma) is crucial**

## Radiation risks

- **Very high dose radiation can have immediate tissue damage and risk of future cancer**
- **Low dose radiation may have increased long term risk of cancer**
- **Most risk models are based on survivors of catastrophic radiation incidents (atom bomb, Chernobyl)**

## Radiation risks

- **Assume linear relationship between radiation exposure and the risk of cancer**
- **Assumes that any exposure, regardless of how low, increases risk of cancer**
- **Greater lifetime risk for exposure at younger age due to greater sensitivity and longer lifespan to potentially develop cancer**

- **BEIR VII (Biological Effects of Ionizing Radiation)**

Lifetime attributable risk of cancer from exposure to radiation  
Number of cases per 100,000 persons exposed to a single dose of 0.1 Gy

Age at exposure	Male	Percent	Female	Percent
0	2563	2.56%	4777	4.78%
5	1816	1.82%	3377	3.38%
10	1445	1.45%	2611	2.61%
15	1182	1.18%	2064	2.06%
20	977	0.98%	1646	1.65%
30	686	0.69%	1065	1.07%
40	648	0.65%	886	0.89%
50	591	0.59%	740	0.74%
60	489	0.49%	586	0.59%
70	343	0.34%	409	0.41%
80	174	0.17%	214	0.21%

Adapted from National Research Council. Health Risks from Exposure to Low Levels of Ionizing Radiation. BEIR VII Phase 2. Washington DC. National Academic Press, 2006

- **Who is at risk:**
  - **Patient / research subject**
  - **General public**
  - **Workers**
    - **Physicians**
    - **Technologists**
    - **Staff**

## Radiation risks

- **How do we protect them?**
  - **Patient / research subject**
    - **Departmental safety policies and screening procedures**
    - **IRB**
    - **Radiation Safety Committee**
    - **Radioactive Drug Research Committee**
    - **Regulatory oversight (Joint Commission, DPH, FDA)**

## Radiation risks

- **General public:**
  - **Shielding of exam rooms from magnetic fields and radiation**
  - **Regulated transport/release of radioactive materials**
- **Workers**
  - **Training and monitoring requirements**
  - **Annual radiation exposure limits**
  - **ALARA policies (As Low As Reasonably Achievable)**

## References

- **Description of procedures, how to prepare for it:**
- <http://www.radiologyinfo.org/>
- <http://www.medicalimaging.org/>
- <http://www.massgeneral.org/imaging/>
- <http://www.massgeneral.org/imaging/services/>

## Acknowledgements