original article

Current trends in perfusion and endoscopic computed tomography imaging

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Abstract

This article explores current trends in perfusion-computerised tomography (CT) and CT endoscopy as described in the literature [1-25]. Issues discussed are the clinical significances of performing these studies, techniques applied, advantages and disadvantages of both examinations, and future direction of the two imaging techniques.

Keywords: Infarct, polyps, intraluminal imaging, extraluminal imaging, CT colonoscopy, CT endoscopy, CT bronchoscopy, virtual endoscopy.

Introduction

Computed tomography (CT) imaging has seen many advances in the past decade, such as the ability to perform helical scanning to sub-second, half- millimeter slice acquisitions. A new dimension currently enjoying wide interest amongst specialists in the field of CT is that of perfusion CT and CT endoscopic imaging. This article focuses on the directions of these two dimensions in imaging studies.

CT perfusion is mainly used to assess the extent of acute stroke in patients. CT perfusion studies are also being used in oncology, and in hepatic and renal perfusion. The main thrust of this article is CT perfusion of the brain but virtual CT imaging of the liver and kidneys is also discussed, albeit briefly.

CT endoscopic imaging is currently applied in imaging of the colon and has also been applied in other areas such as bronchoscopy, gastroscopy and cystoscopy. Virtual CT of the colon is discussed whereas virtual CT imaging of the bronchus, stomach and bladder is covered briefly in this paper.

Perfusion CT of acute stroke

• Clinical significance of this pathology Stroke is a disease where the function of the brain is disrupted as a consequence of interference with blood supply that is usually followed by various sensory loss and motor paralysis. Acute stroke is responsible for a high incidence of mortality in Western countries. Intravenous thrombolysis has proved to be an effective treatment option for acute stroke, provided that such treatment starts within three hours after the onset of the ictus or intra-arterial within six hours [1]. The aim of CT perfusion is to differentiate the infarct core, which presents as irreversible infarcted tissue, and ischemic penumbra - tissue at risk of infarction [2]. This penumbra is found around the infarct core. The aim of thrombolysis is to destroy the clot responsible for the ischaemic event, in order to improve blood flow to reduce mortality [3].

CT perfusion is used as an alternative in institutions where magnetic resonance (MR) imaging is not available or is contraindicated [2]. Research has shown that measurement of cerebral blood flow can predict both the extent and severity of cerebral infarction, as well as clinical outcome, in acute stage of ischaemia. This early assessment of cerebral haemodynamics enables selection of appropriate treatment options to improve outcome [4]. Research findings indicate that in patients with early complete revascularization after proximal middle cerebral artery embolic occlusion, the final infarct volume can well be established by CT perfusion and can be approximated by the size of the initial ischaemic lesion volume [5]. Smaller ischaemic lesions are found to have a higher collateral flow promoting survival of ischaemic brain tissue. CT perfusion can be used to distinguish a complete stroke and transient ischaemic attack further adding to its diagnostic usefulness [6].

• Brain perfusion technique

Various techniques for perfusion CT are described in the literature. Some departments perform a technique where a non-enhanced axial scan is performed from the foramen



magnum to the vertex after which 100 mls of non-ionic contrast medium is administered via a power injector at a rate of 3 ml/sec [7]. Helical scanning commences 25 seconds after

Figure 1a: Unenhanced axial CT scan of a 86 year old female with right sided hemi-paresis. There is evidence of patchy bilateral white matter abnormality but no evidence of acute large vessel stroke. (Reprinted by kind permission from the authors [2]).

the introduction of the contrast medium. Software is used to evaluate brain anatomy, presence of hemorrhage, location and extent of hypoperfused brain regions. The presence of vessel



Figure 1b: A cerebral blood flow (CBF) map created post contrast media administration of the same patient. An extensive abnormality within the left hemisphere is evident (arrowheads). (Reprinted with kind permission from the authors [8]) occlusion can also be determined by construction of CT angiograms [7]. Figures 1a and 1b are of some CT images.

• Dynamic perfusion CT

Some investigators apply a dynamic CT perfusion technique where scanning occurs at a desired level within the brain. Scanning is usually done at the level of the basal ganglia: this level contains representative territories supplied by the anterior, posterior and middle cerebral arteries from Circle of Willis thus visualization of pathologies in all the major vascular territories is possible [2]. Fifty mls of iodinated contrast medium are administered with a power injector via the antecubital vein and 32 to 40 images are obtained at a rate of one image per second to assess the signal intensity change during the first passage of the bolus through the vasculature of the brain. Calculations of the cerebral blood volume (CBV), CBF and time to bolus peak (TP) maps are performed with the necessary software [9].

• Perfusion measurements in acute stroke

Studies to diagnose ischaemic brain areas have used quantitative measurements of various cerebral perfusion parameters such as CBV, CBF and TP. Thresholds have recently been developed for these parameters to distinguish infraction and tissue at risk [9]. CBV can be defined as the total volume of blood in a given region of the brain and refers to the units of milliliters of blood per 100g of brain tissue (ml/100g). The CBV map is obtained by the mathematic integration of the area under investigation versus time curve [10]. CBF is defined as the volume of blood moving though a given brain region per unit time, representing the capillary flow in the tissue. CBF applies units of ml of blood per 100g of brain tissue per minute (ml/100g/min). Normal CBF is between 50 - 60 ml/100g/min. A decrease of CBF below 10 - 12 ml/100g/min is believed to cause membrane pump failure and cell death [10].

Some researchers argue to the contrary, namely the absolute normal values for CBV and CBF may vary widely, depending on technical factors such as the imaging modality, the algorithm used for calculation and the evaluation method [9]. These authors recommend cognizance be taken of this aspect when analyzing such measurements. They further report that CBF and CBV values show an inter-individual variability of greater than 20%. Based on these factors they conclude (i) the calculation of accurate and absolute values becomes impractical, and (ii) the use of absolute threshold for therapeutic decision making becomes impossible, hence rigorous research should be done to quantify or disapprove this statement.

Advantages of CT perfusion

- The advantages include:
- Differentiation of cerebral infarction at early or super early periods.
- Determining the range and size of lesion areas.
- Differentiation of lacunae, cortical branch and deep perforating branch infarction and large cerebral infarction.
- Effectively reducing the high rate of false negative results often obtained with CT [11].
- Perfusion CT can be performed rapidly and conveniently after non-contrasted CT imaging of the brain thus no need to transfer the patient to another unit.
- Range of lesions detected by CT perfusion are greater than conventional CT.
- CT scanners are more readily available compared to MR units, and are usually situated near the emergency departments in many institutions.
- Assisting in the management of patients with acute stroke, as it is more likely, rather than less likely to predict those patients who would benefit from revascularization of the infarcted brain; irreversible brain infarction and reversible infarcted tissue can be diagnosed with relative ease on CT images [5].

Limitations of perfusion CT

The following are considered as limiting factors in the use of perfusion imaging:

- Radiation dose to the patient is higher because up to 40 slices are obtained at a single level in one examination as occurs in dynamic scanning [5].
- There is a limited sample volume; for example multi-slice scanners have a maximum field of view of 20mm restricting the choice of location as only a limited section of the organ of interest can be studied.
- Movement artifacts during repeated imaging cause errors in the perfusion measurements.
- Beam hardening artifacts in any image set can have a significant effect on the final perfusion value.
- More than 15 minutes is added to the scanning time, post processing, and interpretation time, compared to normal non-contrasted scans [6].

Some centers use xenon enhanced CT for noninvasive measurements of cerebral blood flow in ischaemic cerebrovascular disease but this method is not widely applied as only a few institutions have the technology to perform the examination. In addition this technique is also limited because (i) patients experience difficulties when inhaling xenon, (ii) xenon itself is thought to influence cerebral blood flow, and (iii) lack of commercial availability [2].

Future challenges of perfusion CT

There are many unanswered questions in management of CT perfusion. These include:

- Deciding which patients would best be treated with thrombolysis.
- Whether a particular site of occlusion can be successfully revascularized.
- Predicting the development of intracerebral haemorrhage on CT images with and without clinical deterioration [3].

The immediate restoration of flow to an infarcted area cannot be completely ascribed to the application of thrombolytic treatment as inter-related factors such as collateral circulation, ischaemic penumbra, lesion location, extent and time to treatment and haemorrhagic conversion are all variables that may influence restoration of blood flow [3]. It stands to reason that future clinical trials might address most of these concerns in the quest for introducing routine CT perfusion imaging in patients when indicated.

Application of perfusion CT to multi-slice systems would enable physiological parameters to be captured over larger tissue volumes, resulting in the demise of current single slice studies. More sophisticated CT technologies, which vary the x-ray exposure during scanning rotation may allow reductions in radiation dose associated with repeated volume acquisition.

Respiratory-gating could reduce mis-registration artifacts for abdominal functional CT whilst cardiac-gating may facilitate measurements of myocardial perfusion. It is reasonable to postulate that recent developments in electrocardiogram prospective gating techniques, developed for cardiac imaging, may also be extended for use in reducing respiratory motion artifacts [6].

Oncology, renal perfusion, and hepatic perfusion

Although there are limited data available the role of perfusion CT in oncology and in renal and hepatic studies is briefly discussed.

Perfusion CT in oncology is used to detect whether tumour shows an increase in perfusion levels, indicating the presence of neovascularization, namely angiogenesis which is the formation of collateral blood supply on which tumours thrive [6]. CT perfusion is used to determine anti-angiogenetic therapy, [prevention of revascularization]. Currently perfusion CT is used to assess tumour grade in-vivo and can effectively reduce the potential for sampling error by enabling use of biopsy-guidance to the tumour region most likely to be the highest grade. CT perfusion may also be of value when biopsy is difficult or when there is a propensity for tumour grade to change with time. In view of the relative invasiveness of cerebral biopsy, perfusion CT methods have also been used to assess grade of cerebral glioma thereby avoiding actual cerebral biopsy and subsequent risks associated with cerebral or other biopsies [6].

Research in the use of perfusion CT imaging of the kidneys is ongoing and it is anticipated that findings of such studies will be published in the near future. In assessing renal perfusion with electron-beam CT, perfusion measurements can be obtained by simply centering the dynamic acquisition region of interest over the kidney after administration of contrast medium used to visualize abdominal organs [12]. Time attenuation curves are then calculated from the transverse dynamic scans data using appropriate software. The data are then used to calculate cortical perfusion, cortical peak height and cortical peak time. It is thought that evidence of abnormal low perfusion in stenotic kidneys may have predictive value for renal atrophy and may constitute an indication for revascularization. Time attenuation curves may help distinguish renal artery stenosis with/ without preserved perfusion [12].

Due to new helical CT software, multi-phasic imaging of the liver has become popular and this includes perfusion imaging. The literature reports one study done to assess CT perfusion of the liver to establish whether patients at risk of developing hepatic metastases could be identified with perfusion imaging. Results were inconclusive as to the latter but it was found that patients with hepatic metastases had an increased hepatic arterial flow relative to portal venous flow [13]. Perfusion parameters that may be investigated include liver perfusion, arterial fraction, distribution volume and mean transit time. This technique assesses the hepatic inflow rate based on the dual input, single compartment model of the liver circulation.

Future developments of perfusion CT

These are expected to include:

- Liver perfusion software that calculates the standardized perfusion values (SPV), analogues the standardization uptake value used in positron emission tomography (PET).
- New image acquisition protocols that will enable measurement of multiple parameters in one examination.
- Development of new contrast media that have longer intra-vascular residence time which would overcome some of the complexities of physiological modeling required for conventional contrast media.
- Integrating PET with CT systems creating opportunity for measuring glucose metabolism or other physiological processes. This combined imaging may be useful for in-vivo investigation of the complex relationship between angiogenesis and glucose metabolism in ischaemic tissue and tumours [6].
- The potential to further the clinical value of existing methods should such tested clinical trials be validated since CBF and mean transit time (MTT) methods have not been extensively investigated with CT perfusion [10].

Other future trends possible by perfusion CT are: • Stereotactic biopsy guidance. Distinguishing radiation necrosis from recurrent glioma and determining prognosis and response to treatment [10].

CT colonography

• Clinical significance

CT colonography has been extensively researched and used to detect colonic polyps and cancers. This technique uses volumetric CT data combined with specialized imaging software for detecting pathologies such as colonic neoplasms or polyps as most colorectal cancers arise from pre-existent adenomatous polyps. The detection and removal of these precursor adenomas will result in a decrease in the incidence of, and mortality rate of, colorectal cancers [14]. This imaging method promises to become a primary method for colorectal screening. Results from studies done show that the accuracy of CT colonoscopy is comparable to that of conventional colonoscopy for the detection of polyps greater than 10mm [15, 16]. However, the use of CT colonoscopy as an alternative to conventional colonoscopy requires formal evidence-based scientific data [15]. This means that the efficacy of this method will have to be proven by large-scale clinical trials before it can be widely applied as a diagnostic tool. This view is shared by other authors who argue that due to the absence of scientifically proven data, the usefulness of CT colonoscopy as a screening tool remains unproven to date [17].

Preliminary results from clinical trials comparing virtual colonoscopy to conventional colonoscopy indicate that the sensitivity of virtual colonoscopy ranges from 75 - 100% and 86 - 90% for identification of polyps greater than 10mm. Endoscopists argue that virtual colonoscopy is unable to detect polyps 5mm or less in size and that conventional colonoscopy is reported to have a miss rate of 24% for such lesions [18]. Virtual colonoscopy is therefore thought not to compare unfavorably to the latter. Virtual colonoscopy further allows patients to obtain reliable non-invasive information on the status of their colonic mucosa thereby allowing the patients to make an informed decision whether to proceed to conventional colonoscopy for polypectomy [19].

• CT colonoscopy: the technique

Patient preparation as describe in the literature is very similar to conventional barium studies, namely standard bowel preparation that consists of:

- Low-residue diet on the day before an examination.
- Oral sodium phosphate, about two liters, on the night before and on the morning of an examination.
- Oral iodinated contrast agent administered at least two hours before helical CT scanning.
- One mg of intravenous glucagons is administered after the patient is positioned on the CT table, and the colon

is distended either with air or carbon dioxide gas [18].

A scout image is obtained after which single breath hold acquisitions are obtained in the supine and prone position. Acquisition of images entails 1,25 - 2,5mm collimation with a 13,5- 5mm/second table speed, 1mm reconstruction intervals with exposure factors of 120 kVp and 100 mAs. Total examination time is about 10 minutes or less [17].

• Image acquisition and analysis

After acquisition and interpolation of raw helical CT data, images are reconstructed with sufficient overlap to optimize 3 dimensional (3D) image display [20]. Certain software allows multiple image display techniques to view helical CT colonographic data. Review of interactive 2D multi-planar reformation of the entire colon is now possible, with simultaneous viewing of the axial, sagittal and coronal planes. Focal abnormalities detected in one plane can be cross-registered simultaneously to the other two planes [20].

Image processing and interpretation are performed using available CT colonoscopy software. Options possible with this software are:

- Electronic cleansing of residual luminal fluid. Advantage of the electronic fluid cleansing method is that polyps submerged in fluid can now be detected as this fluid is electronically removed by subtraction [17].
- Stool tagging for CT colonoscopy is applied to avoid colon purgation.
 Adherent stool represents the major cause of false-positive findings in CT colonography. Barium tagging of adherent stool increases the specificity for true polyps on CT colonoscopy. Barium tagging of a true colonic polyp is the main pitfall in solid stool tagging.
- Virtual fly-through of the volume rendered 3D images along an automated centerline path.

Other post-processing options available with CT colonoscopy are:

- Panning through 2D multi-planar slices
- Navigation through computer simulations of the colon with the assistance of flight-path planning algorithms
- Splitting or unfolding colon models
- Computer-assisted polyp detection [18]

Figure 2 is an example of the various software options currently available with CT colonography.

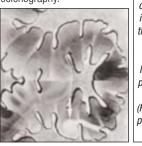


Figure 2: Transverse longitudinal image of the superior and inferior surfaces of the colon as though the colon were opened along its longitudinal axis. A pedunculated polyp is visible (arrow). (Reprinted with kind permission from the authors [14]) Most studies have relied on 2D CT images for primary polyp detection, reserving the 3D rendering for confirmation or problem solving. The advantage of 3D CT colonoscopy over 2D imaging is its improved depiction of surface morphology, particularly in distinguishing polypoid lesions from haustrial folds [17]. Conspicuity of the polyp is greatly increased using 3D endoluminal perspective for primary detection. Although less sensitive for initial detection, the complimentary 2D images improve specificity and are therefore indispensable for distinguishing true polyps from a variety of pseudo-polyps as seen in 3D imaging.

Figures 3 and 4 show the difference in 2D and 3D images obtained with current CT colonoscopy software. Note the excellent endoscopic detail



Figure 3: Demonstration of the fat internal attenuation of a lipoma (arrow) which was confirmed with colonoscopy. (Reprinted with kind permission from the authors [14])



Figure 4: demonstrates the 3D version of this image as a nearly obstructing intraluminal mass indicated by the arrows. (Reprinted with kind permission from the authors [14])

obtained with this 3D algorithm. It has been shown that in spite of all these advances, polyp detection can be just as effective using 2D images as by using 3D endoluminal images but each is complimentary to each other [14]. Consensus exists amongst experts that inspection of 2D slices is sufficient for identifying possible lesions and that 3D imaging is useful for resolving suspicious polyps from anatomical variants [18]. An important aspect is that original data (scans) should also be analyzed to identify incidental findings possibly responsible for the abdominal symptoms as incidental findings reportedly have a high rate as indicated elsewhere in this study [18].

Another new development is that of hybrid rendering. This method combines the imaging characteristics of surface rendering and volume rendering simultaneous in a single image. This provides excellent detail of the anatomy of the colon as it provides an image relative to the actual anatomy of the colon.

The two 3D rendering techniques that can be applied by CT colonography are:

- Surface rendering, and
- Volume rendering [18]

Figure 5 demonstrates a reconstructed volume-rendering image where the mucosa appears as a translucent membrane with a thickness of 1 - 3 voxels [21]. Surface rendering identifies surfaces from an endoluminal perspective thereby reducing the data to a set of surface triangles. Volume rendering displays extra-luminal soft tissue and attenuation data. None of the two methods is said to be superior to the other [14].



Figure 5: Reconstructed volume-rendering image. (Reprinted with kind permission from the authors [21])

Advantages of CT colonoscopy

These are:

- The dose from combined supine and prone scanning is approximately 20% lower than the dose of a double contrast barium enema thereby giving it a marginal advantage over barium enema studies as a screening tool.
- Incidental findings often diagnosed by CT colonoscopy have a slight advantage over conventional colonoscopy which benefits the patient since earlier treatment can be applied where necessary to such pathology findings. Interesting to note is that 11% of patients were found to have highly significant incidental findings.
- Interpretation time has now been reduced to 15 minutes per examination.
- Patients are also reportedly more willing to return for their CT colonoscopy compared to the compliance rate of conventional colonoscopy or barium enema [14].
- Data presented at the first international symposium on virtual colonoscopy in Boston (USA) indicate the performance of virtual colonoscopy for detection of colonic polyps and cancers, approach those of conventional colonoscopy and exceed those of barium enema [23].
- Forward and rear view 3D visualization of surfaces of haustrial folds is not possible with endoscopy [20].
- CT can be used to complete the colonoscopy in patients with incomplete colonoscopies due to obstruction, as patients would have had their bowel preparation. CT colonoscopy can thus image beyond the point of obstruction, which is a major additional advantage [24].
- Patients can return to work immediately after the examination because sedation is not needed.
- No reported complications for CT colonoscopy to date.

- More accepted by patients as less intervention is needed [14].
- Virtual colonoscopy has decreased discomfort and inconvenience, reduced costs and risks compared to conventional colonoscopy. But in spite of these advantages, CT colonoscopy must first overcome several political, economic and social hurdles before becoming a commonly applied examination such as acceptance by endoscopists and referring practitioners [18].

Disadvantages of CT colonoscopy

These are:

- It is often a tedious procedure and is prone to error of interpretation because a physician must navigate the entire colon to visually search for lesions.
- The presence of residual faeces may simulate polyps or masses and retained fluid can obscure subtle lesions.
- Collapsed segments of bowel during scanning may conceal or mimic neoplasms.
- Normal visual cues, such as mucosal colour changes indicating pathology found in conventional colonoscopy, are not visible with CT colonoscopy [18].
- The main barrier to 3D endoluminal imaging has been its time consuming nature [17].
- Inadequate insufflation of specific parts of the colon is a particular disadvantage [20].
- Additional prone position to best distend all portions of the colon increases the radiation dose.
- Removal of polyps or histology sampling is not possible with CT colonography.
- Software can be expensive even though prices are coming down [20].

Future trends

New trends in CT colonography include:

- An image analysis algorithm used to view large segments of the colon in a single image that can be inspected rapidly.
- Display of the colonic mucosa as a flat surface [14].
- Auto-navigation where navigation through the tortuous colon will be undertaken automatically using software.
- Computer-aided diagnosis providing a framework to the radiologist in the detection of focal wall abnormalities, thereby improving sensitivity and time efficiency. Abnormal areas will be highlighted by the computer allowing closer inspection of such electronically noted areas [20].
- Development of contrast agents that are either absorbed or secreted differently by normal and abnormal areas of bowel wall remains a research challenge [18].

Gastric CT endoscopy

This is a new area currently being explored thus limited data are available. Studies done to compare the usefulness of CT endoscopy of gastric lesions with 3D virtual display and conventional barium meal studies have shown that virtual endoscopy proved helpful in identifying both intraluminal and submucosal components of the stomach, an aspect not at all possible with conventional endoscopic examinations [25]. Findings of this study suggest that 3D CT virtual endoscopy performance is similar to that barium studies but that conventional endoscopy is significantly superior to CT endoscopy. For gastric polyps, barium studies and endoscopy are marginally superior to 3D CT endoscopy. However, for other diseases such as submucosal tumours and gastric varices, 3D CT performances are similar to conventional barium studies or conventional endoscopy. The major pitfall of 3D CT endoscopy is that it is unable to detect subtle mucosal changes visible with endoscopy. The ability to simultaneous evaluate mucosal changes and extraluminal abnormalities, is a unique advantage not achieved with endoscopy.

CT bronchoscopy

Few investigators have applied this technique hence in-depth discussion of this technique is beyond the scope of this article. However, the advantage of CT bronchoscopy is its ability to delineate endobronchial pathology sites rather than pathology not detected by bronchoscopists [22]. This examination is done as an adjunct to bronchoscopy and is not considered to be in competition to bronchoscopy. This is particularly so as most pathologies present in the bronchus can be seen with ease via a bronchoscope. Figures 6 and 7 illustrate this method of examining the bronchus/mediastinum.



Figure 6: Sub-carinal lymph node is highlighted; about 2 cms at the level of the carina. (Reprinted with kind permission from the authors [21])



Figure 7: Virtual CT bronchoscopic image not possible with bronchoscopic software. On this image the locations of 3 biopsy sites chosen by three pulmonologists without lymph node highlighting,

indicated by the (X) and with lymph node highlighting, indicated by the (_), is demonstrated, adding another benefit to imaging and biopsies of peri-bronchial lesions. (Reprinted with kind permission from the authors [22])

Advantages of CT bronchoscopy:

- Assists bronchoscopists in directing them in terms of biopsies through normal mucosa, or difficult sites.
- The airway distal to the tumour site (obstruction) can be evaluated.
- Endoluminal as well as extraluminal imaging can occur via shaded surface display and volumetric display modes. This allows intra and extra visualization of the bronchus [22].

Virtual cystoscopy

Another new area currently being explored by virtual CT is that of virtual CT cystoscopy. Studies

Conclusion

Research shows that CT perfusion has a major role to play in imaging of acute stroke. It is postulated that this role will be further developed and CT perfusion will therefore remain an investigation of choice to depict extent of and nature of necrosis in debilitating acute stroke. Perfusion imaging therefore redefines the role CT plays in depicting vascular physiology in addition to detailed anatomy. It would appear that the sky is the limit as intrinsic topography of structures and physiological processes can now be viewed with depiction of excellent anatomical detail using a relative simple CT examination [6].

Based on the future challenges identified it would seem that CT endoscopy will have more challenges to overcome compared to that of perfusion imaging. Further validation of CT colonoscopy will have to be proved by large scale multi-institutional trials [20]. If it can be shown that the accuracy of CT colonoscopy can approach that of colonoscopy for polyp detection smaller than 5mm, then CT colonoscopy could potentially replace endoscopy. Its future role will remain especially in imaging of obstructive pathologies where fibre-optic scopes cannot pass. Rigorous research is needed to validate these two new imaging options as the latest trends in CT.

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