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Advanced image processing in radiology

A TODD-POKROPEK

Department of Medical Physics, University College London, Gower Street, London WC1E 6BT, UK and INSERM U494, Paris, France

It is clear that radiology is in the process of making a transition between "analogue" imaging and digital imaging. While this has the benefit of enabling electronic retrieval, archiving etc. (the picture archiving and communications system field which is covered elsewhere in this issue), the data are also available for use in so-called advanced image processing. However, the aim of image processing should not be just to produce prettier pictures, but to extract good clinical information, and a legitimate question is — is advanced image processing in radiology required? However, advanced processing methods need to incorporate clinical knowledge and be defined using clinical constraints. The continuing advances in hardware performance have made many previously computationally unattractive methods feasible, an example being iterative reconstruction in tomography, which is now routine in nuclear medicine, but not CT. Both linear and non-linear operations can be considered, including the important topic of model fitting, where two classes of method are important: data driven and hypothesis driven. Examples of data driven methods are principal component analysis, factor analysis and independent component analysis, where the model is derived from the data. Hypothesis driven methods are all implicitly or explicitly based on model fitting; a preliminary data driven step followed by hypothesis driven approaches which could be called constrained statistical image analysis. Examples are shown as used in nuclear medicine and MRI. Another important problem in radiology is that of multimodality image registration and fusion. In the analysis of such data, tests against reference data sets (atlases) are required, normally requiring warping the data sets in space, for example by the use of optic flow, or some kind of diffusion equation. Real-time analysis of data during acquisition can lead to optimization of acquisition procedures, which is an example of intelligent image acquisition. Incorporation of such image analysis techniques into a decision support system is highly desirable. The availability of distributed image processing and data, usually called "grid" computing, is likely to significantly change the types of methods used and their availability.

Summary

- Radiology is in the process of making a transition between "analogue" imaging and digital imaging and between two-dimensional and three-dimenstional imaging.
- Advanced processing methods need to incorporate clinical knowledge and be defined using clinical constraints.
- Two classes of method are important: data driven and hypothesis driven.
- In the analysis of such data, tests against reference data sets (atlases) are required.
- The availability of distributed image processing and data, usually called "grid" computing, is likely to significantly change the types of methods used and their availability.

The advances in computer hardware over the last decade are remarkable. We can note a gain in speed of conventional personal computers of about a factor of 20 over the last 3 years. The progress seems to be continuing into the future. This gain in performance has made possible many new methods, which previously could not be contemplated at least in routine, now practical. One change which can already clearly be observed is the change from two-dimensional (2D) imaging (for example of CT slices) to 3D acquisition and volume display, as a result of the impact of spiral CT scanners (and advances in MRI and ultrasound). However, this improvement in performance has been accompanied by, or has resulted in, a considerable increase in the quantity of data available, a good example being from single cardiac transaxial slices to gated 3D acquisitions in MR and ultrasound and CT. However, a key requirement is not just to do something faster, but to perform a task that will enhance the value of the results.

One specific issue has been with respect to the use of parallel processing computers, as opposed to conventional serial machines, where progress in the latter has made the use of the former redundant. Indeed, it has been suggested that for certain very large problems, it might be better to wait for the improvement of speed of hardware in order to complete the task faster than tackling it straight away on current slower hardware! Of course the improvement in hardware has also been accompanied by an increase in the overhead used by operating systems and certain well known packages where no perceptible gain in performance is obvious to the end user. However, this limitation does not normally apply to image processing tasks required in radiology, which are much more computer intensive than for example a word processor, and real gains can be achieved.

A second issue has been the incorporation of smart processing as part of the (intelligent) acquisition stage of various devices, incorporating microchips, such as DSP processors within the signal processing components of the detectors. It has as a result been difficult to distinguish pure acquisition from pre-processing, and to provide a clean interface between acquisition and processing.

Advances in conventional image processing and image reconstruction

Having acquired good data, we need to do something with them. Conventional image processing includes such operations as noise reduction, segmentation and region identification, and image display. Transforms and filters form very basic image processing tools (see for example [1]). Essentially one chooses an appropriate set of basis function (for example sinusoids), a transform (for example Fourier) and then one filters the "eigenvalues". Filtering is just the process of reconstituting the modified version of the original data as being a weighted set (the filter) of the eigenvalues multiplied by their corresponding basis functions. While this is well understood in the Fourier frequency domain, such operations may be generalized by choosing other basis functions, for example as in the Karuhen–Loeve transform. In addition the process may include constraining the filtering process by methods which may be called regularization. The aim of the filtering process is normally to alter the properties of the image, for example the noise characteristics. Such a filtering operation is linear, but non-linear methods such as anisotropic blurring are also of considerable interest. An example of considerable interest, for example for detecting change, is that of Kalman filtering [2, 3].

Tomographic reconstruction is an example of the solution of an inverse problem, which is another basic tools in image processing [4]. Here the key feature is to set up a good forward model relating any set of solutions; in CT the attenuation map (electron density distribution) **A** in the patient or object, and the observations **O** that these would generate. This may be expressed in matrix notation

$$\mathbf{O} = \mathbf{F}\,\mathbf{A}$$

where **O** and **A** are normally given in vectorized form and **F** is termed the forward model or operator. The problem is then to choose a good method for solving this rather large set of simultaneous equations. At present the most common method of performing this task in CT is by filtered backprojection, but an iterative method such as maximum likelihood expectation maximization (MLEM) or ordered subset expectation maximization (OSEM) should be a considerable improvement using an equation of form:

$$a_j^{n+1} = a_j^n \sum_i f_{ji} \left[\sum_k f_{ki} a_k^n \Big/ o_i \right]$$

where n is the nth iteration, a_j is the jth element of the guessed solution **A**, f_{lm} is an element of the forward operator and o_i is the ith element of the observations **O**. In reality, this operation is relatively easy to understand. An iterative approach is used where a^n is the current guessed image. The expression between the square brackets is just the ratio of the prediction of what the observed data would have looked like, coming from this guessed image (that is the forward "projected" guesses) divided by the real observed data. If this ratio is one, then the guess fits the observation. However, this ratio of observations needs to be converted to corrections for the pixels in the image, which is performed by the term preceding the square brackets. The resulting value is then used to modify the current guess at the corresponding pixel. This continues until we find some good reason to stop (which is not as easy as it sounds). Two standard methods are used: MLEM and OSEM, where the advantage of the latter is faster convergence. Both methods are considerably better in terms of signal to noise ratio and the reduction of artefacts than conventional filtered backprojection, but are at least an order slower. However, progress in computing (Moore's law) suggests that this should not remain a problem for very much longer. However the dramatic increase in volume of data resulting from, for example, spiral CT goes in the other direction. Spiral CT data also require some additional refinements to produce high quality isotropic data, in particular when working with images after contrast medium injection.

Another mathematical technique called regularization can be used to impose additional constraints to the solution and can be very helpful [5]. A typical form of regularization is to minimize not just the fit, *i.e.* the distance, between observations **O** and the corresponding solution values generated, which were generated from the guessed solution (**A**) by applying the forward model (**F**), but also, at the same time, minimizing some property of the reconstructed image or solution, for example its smoothness. This is normally obtained by applying a regularizing operator (**R**) to that solution, for example an estimate of smoothness. A common form for the operator **R**[] is to look at a derivative, for example the first or second. Thus we find the best solution in the least squares sense which is also the smoothest, for example. Regularized reconstruction can be of help where noise levels are high, for example in nuclear medicine, but also where data are undersampled, for example cardiac MRI. Computing time–activity curves or uptake rates for contrast medium in CT and MRI can be performed more accurately indirectly by use of the original raw projection data, rather than by defining a region of interest on the reconstructed data and deriving the time curve directly from the reconstructed sequence. This has particular interest in non-linear (model based) imaging applications such as electrical impedence tomography, optical tomography and even attenuation correction in nuclear medicine.

Image processing and the imaging chain

Image processing occupies only one part of the imaging chain, as illustrated in Figure 1. The imaging chain starts with acquisition and preprocessing to make good clean data available. Image processing as such is a precursor to the stage of image interpretation and decision making. This process has to be integrated within a system of validation and evaluation. Finally other data than images need to be integrated.

Thus the aims as such of image processing can be described as firstly detection, secondly measurement and hence, finally, description. While the problems of detection have often dominated the area of medical image processing, the problems of image interpretation are in the process of becoming considerably more important. This may be illustrated by some examples. One such example is in the handling of lung/liver CT scans looking for small lesions, or, in nuclear medicine, sentinel node images. Small lesions and sentinel nodes may be detected by some kind of matched filter, giving the probability a particular feature has of being the object we are trying to detect. It should be noted that information other than intensity variations may be of value, for example texture. It is well known that the human eye is rather insensitive to variations in texture, and additional information may be obtained by detecting changes in other features of the image than grey scale intensity; an example applied to nodule detection and characterization in CT images is indicated in Figure 2. The second stage is that of measurement: of what size, where in the structured object are they found, perhaps also looking at their shape and texture. This leads an attempt to determine a description: benign/malignant. The improvement of signal to noise ratio requires a filter, which as previously indicated implies a constraint and a model. The derived description is itself a model. A second example is that of tumour staging, where initially we have the problem of finding the tumour, then measuring its volume and invasion and perhaps change in size with time, finally that of classification, determining its "stage" from which a diagnostic strategy can be planned. Follow up of tumours, in particular of therapy, also requires quantitation.

The integration of image processing, for example within a decision support system, requires forward and backwards inference in the process of evaluation to what may be called a goal (the clinical decision). Goals can be divided into sub-goals and indeed exclusions ("this" information is incompatible with "that" statement). A knowledge hierarchy exists, going from high level such as the clinical condition, to intermediate knowledge such as the description of organs or tumours, down to low level knowledge such as that associated with blood vessel.... This topic is still the subject of active research. Thus while conventional image processing is often about enhancing edges and performing operations on pixels or voxels, advanced

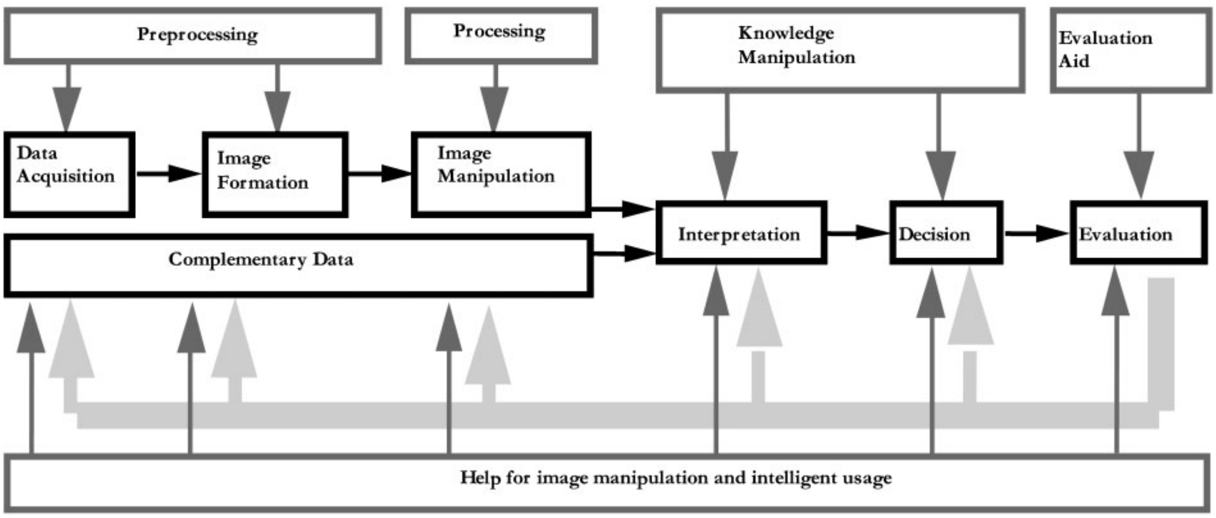

Figure 1. The imaging chain from acquisition to evaluation.

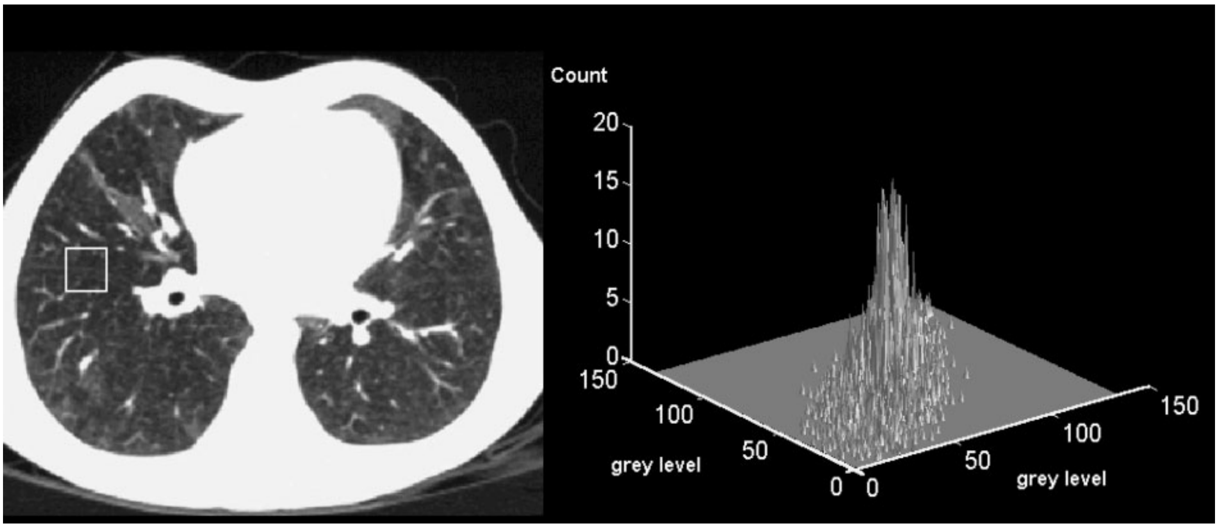

Figure 2. Texture analysis applied to CT data: a window into the CT image looking for nodules (left) and the corresponding co-occurrence matrix used to assess texture (right).

image processing is about performing operations on structures and extracting knowledge.

Functional (physiological) images

One form of knowledge is about anatomical structures, another is related to physiological information. Extraction of physiological information (after appropriate anatomical identification) is clearly becoming of increasing importance and utility, and is a target of advanced image processing tool development. An example of particular physiological parameters of clinical value are estimates of regional cerebral blood flood (rCBF). The aim of extracting physiological data is one of the purposes of the generation of so-called functional images, which is in fact a form of "logical" data compression, reducing the dimensionality of the data. Here a technique such as projecting the raw data against some axis is implied. For example, and trivially, projecting the data against the time axis merely sums the data in time, and projecting a 2D image in time against the y (vertical) axis gives rise to a conventional functional image often used in nuclear medicine. However, this projection can be performed against some (relatively) arbitrary axis or axes in the acquisition (raw data) hyperspace, after an appropriate rotation. This is the area of principal component analysis (PCA) and various alternatives such as factor analysis [6] and independent component analysis (ICA) [7]. The model is extracted from the data themselves.

In addition, when any quantitative value is to be extracted, this always implies the existence of some underlying model, against which we perform some kind of fit using the observed data. An example might be to determine the extraction efficiency of the kidney by fitting the temporal changes in the concentration of a tracer with one or more exponentials and using the derived coefficient as a measure of glomerular function. The underlying model here can be clearly expressed as a compartmental model. The accuracy of the quantitation will still depend on the validity of the model. A specific example of this is in the fitting of a model to that part of an acquisition where only uptake occurs in an organ without any outflow, namely a Patlak plot [8].

Thus an aim of such image processing techniques is to reduce the total amount of data, and make significant data more clearly visible. This implies the use of appropriate (clinical and physical) constraints, which we may also think of as the use of boundary values and models.

Model fitting: data driven *vs* hypothesis driven methods

Hypothesis driven methods take the data that were observed, and generally test the hypothesis. Data driven methods (sometimes called data dredging) take the raw data and, by means of various manipulations, attempt to suggest hypotheses. For hypothesis driven methods we find a (null) hypothesis and generate a statistical test. For data driven methods, we look at the data and suggest a hypothesis (with an estimate of its statistical likelihood). In both cases constraints are required such that we limit the search space and investigate hypotheses based on *a priori* knowledge. These we can call the boundary conditions, for example based on physical limits, spatial extent, (frequently) positivity, the initial/final states, the statistical variation to be expected on both a regional basis and from deterministic knowledge. This is related to the classical difference in approach between statistical pattern recognition [9] and syntactic pattern recognition [10]. Physiological (and anatomical) constraints can also be imposed.

An example of a model based constraint is that of fitting the edge of the cavity of the left ventricle in a series of slices, for example from cardiac images in CT, nuclear medicine or MRI. The conventional image processing methodology will take a single slice, fit an appropriate contour and then proceed to the next slice. However, not only is it known that from slice to slice there can be relatively little change, but the general form of the cavity and its shape over many slices can be predicted. The incorporation of such a model can enormously enhance the power of the fitting process, provided that the model is sufficiently well defined to incorporate both normal anatomy and pathology [11].

Thus included within the class of knowledge based methods are: shape description such as point description models; skeletonization; circumference definitions based on chain codes; Fourier descriptions; and snakes [12]; and further extensions of these into scale space methods such as (3D) multiscale medial axes [13].

The handling of temporal data is a special class of 3D data processing where one is looking for change, that is looking for a derived function. Kalman filtering is a way of assessing the significance of change [2, 3]. We may consider the set of time curves for every pixel. There is a duality between the curve and image data sets. Data compression may be achieved by projection to remove redundancy by reducing dimensionality. Thus we may project against time (summation), against the y (vertical) axis, or choose some oblique axis, as was illustrated in Figure 1. However, constraints are certainly required (*a priori* information). Factor analysis is an example where initially a decomposition into principal components (or axes) is followed by an oblique rotation (based on constraints) [6]. We may display images (eigenfunctions) and curves (eigenvalues); an example from nuclear medicine is shown in Figure 3. Often this is followed by a process of segmentation, model fitting and quantitation. Thus the regions determined by the data driven method are then used to form a model for the hypothesis driven extraction of quantitative parameters. Such methods have also been extended into spectral analysis and can be used for example for scatter correction in nuclear medicine and the generation of synthetic (T_1, T_2 weighted etc.) images in MRI.

Quantitation is one of the aims of image processing in radiology. In general quantitation can be absolute, for example to obtain physiological parameters such as rCBF. In nuclear medicine, to measure absolute activity concentration (Bq.cc^{-1}.) requires measuring activity, volume and then calibration, and is far from easy to perform. Measuring physiological activity from the resultant change in blood flow (the BOLD effect) is likewise indirect. However, in many

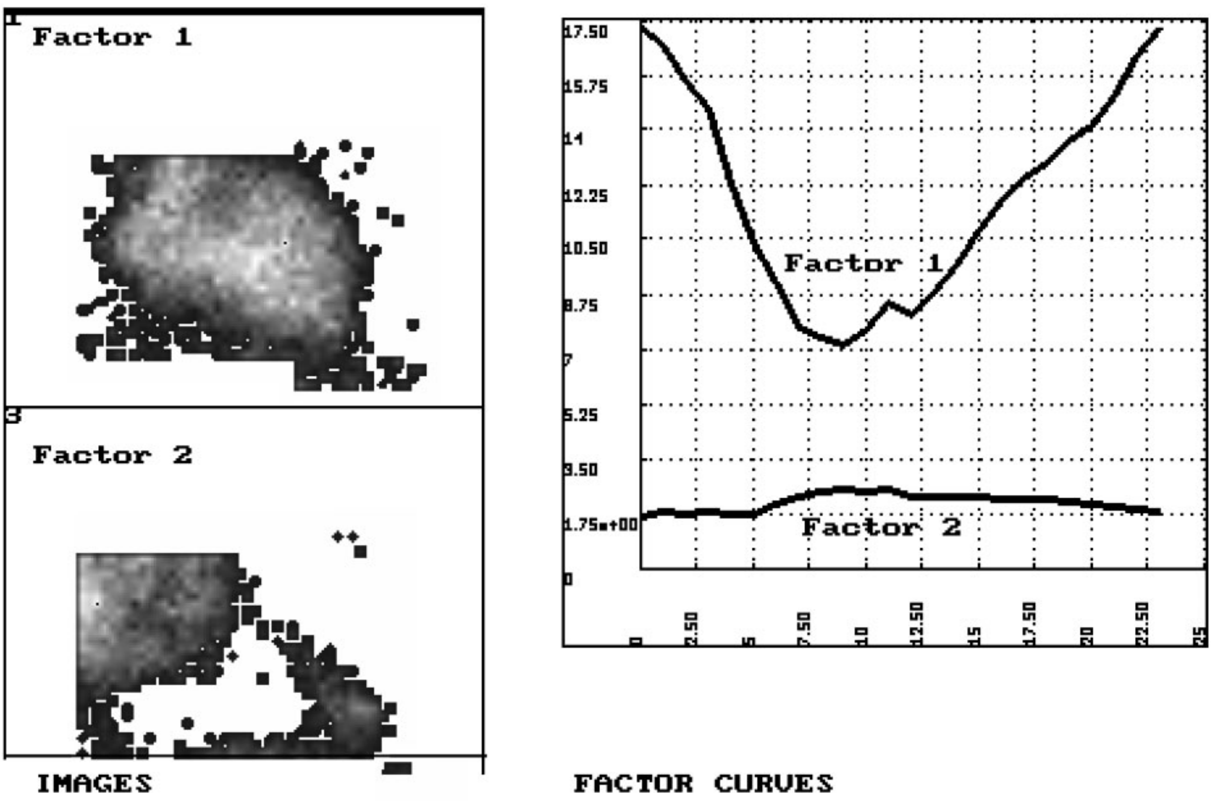

Figure 3. An example of factor analysis of a cardiac image in nuclear medicine showing the first (most significant) factor (above, left) the factor image (weights) and (right) the factor curve, typical of the left ventricle; while below is show the second factor showing out of phase activity and indicating a region of abnormality in the apex of the left ventricle.

cases relative quantitation, comparing values at different sites (for example using symmetry) at different times, or by comparing data between different cases (normal *vs* abnormal) is in fact the normal clinical paradigm and hence requires considerable experience, *e.g. a priori* knowledge. A considerable aid in the area of quantification and the extraction of physiological information is image registration and fusion.

Fusion and registration

Image fusion may be defined as the task of comparing data from different sources, or at different times/procedures so as to extract (and display) common information. Normally a prerequisite is that of image registration, that is ensuring that points in (*n*-dimensional) space in the data from the first source can be mapped into corresponding data from the second source. There are many different methods as described in various review papers [14, 15] and in another paper in this issue.

Registration is a precursor to image fusion and a very general and important annex problem which is: how to interpret the significance of an observation. Two common questions asked are: when I observe a change of some value at a target point (the target selected by the observer, what is the significance of this change? A second question might be more global: show me all the regions where a significant change occurs. Both questions require an assessment of significance which normally requires comparison against an atlas, that is a "map" of expected values and associated properties, *e.g.* SD, bias, positional variation etc. This can then be used to calibrate the observations against an extended data set, which in principle should contain information not just about normals, but also about the various classes of abnormality which might be expected. This requires the building of clinical atlases. An alternative might be to use an internal reference, for example symmetry or time. The building of atlases requires: registration, warping, and where possible both normal and abnormal data [16, 17]. This is an area of active research and the incorporation of non-rigid deformation, in particular, for objects outside the brain, is increasingly used, and requires the additional computer power now available.

Evaluation validation and eHealth

There is considerable interest worldwide and in Europe about the development of eHealth systems, that is computerized systems based on advanced information technology to provide enhanced facilities for healthcare. Image processing in medicine and in radiology is included in such initiatives. A current European project proposal (EU Framework 6 project "BioMedIma") stated that: "during the past decades world leading academic partners in Europe have developed a vast body of knowledge and technology for computer-aided diagnosis, image-guided therapy and biomedical research" of which "a very limited proportion has found its way to the clinical practice and has been integrated into commercial products". The many very sophisticated methods which have been developed need tools for comparison and validation of image analysis methods using standardized image databases.

There is a clear need to provide tools such as a grid-enabled, extendible software platform to enable the integration of existing and emerging image processing technology, to collect and exchange image data, to create an environment for rapid-prototyping, technology transfer and commercial product development, to integrate a library of existing medical image analysis modules into the software platform and to facilitate access to medical and biological images in general. The purpose of such tools would be to provide methods not just to validate the many advanced processing methods that have been described, to ensure that they perform as suggested, are robust when used on different types of data, in particular in cases of pathology, but also to provide tools so that such methods can be disseminated and widely used, not just in research labs but in real clinical practice.

Conclusions

This paper has only considered a very limited range of advanced image processing techniques available in radiology. One important area considered elsewhere in this issue is that of tools for computer assisted intervention and surgery. In all such procedures, evaluation and feedback is a critical issue. It is important to establish: what was the objective, has it been achieved, and what is the impact, *i.e.* does it change management? The feedback loop should optimize the procedure in terms of the cost and the benefits. The fundamental paradigm is to find an appropriate problem, a good solution and then validate it! It would be desirable if this feedback loop were automated and included directly in the image processing chain as such.

In summary, image processing in radiology can lead to an enhancement in the ability to obtain real clinical information. Three important areas of special importance are being developed as a result of increased computing power available. One is the evaluation of significance using tools such as clinical atlases. The second is that of real-time image processing and analysis, enabling smart acquisition where not only is the data pre-processed during acquisition, but the acquisition is itself controlled to ensure adequate (hopefully optimal) data acquisition is performed with respect to the clinical objective. This can be termed smart data acquisition. Finally, the incorporation of such image analysis within a clinical decision support system is also of great potential value [18] and is covered elsewhere in this issue. The success of "advanced image processing" in radiology will occur when, as for the use of "advanced imaging acquisition" methods such as CT and MR, such tools are considered as part of the normal facilities available within any radiology service and not considered to be in any way exceptional.

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