Convergence and Technologies: *Resource Report*

Cancer Research

LIFEx: A Freeware for Radiomic Feature Calculation in Multimodality Imaging to Accelerate Advances in the Characterization of Tumor Heterogeneity

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Abstract

Textural and shape analysis is gaining considerable interest in medical imaging, particularly to identify parameters characterizing tumor heterogeneity and to feed radiomic models. Here, we present a free, multiplatform, and easy-to-use freeware called LIFEx, which enables the calculation of conventional, histogram-based, textural, and shape features from PET, SPECT, MR, CT, and US images, or from any combination of imaging modalities. The application does not require any programming skills and was developed for medical imaging professionals. The goal is that independent and multicenter evidence of the usefulness and limitations of radiomic features for characterization of tumor heterogeneity and subsequent patient management can be gathered. Many options are offered for interactive textural index calculation and for increasing the reproducibility among centers. The software already benefits from a large user community (more than 800 registered users), and interactions within that community are part of the development strategy.

Significance: This study presents a user-friendly, multiplatform freeware to extract radiomic features from PET, SPECT, MR, CT, and US images, or any combination of imaging modalities. *Cancer Res; 78(16); 4786–9. ©2018 AACR.*

Introduction

Texture analysis has been suggested since the early 1980s as a way to extract relevant information characterizing tissue types from various medical images. Recently, there has been renewed interest in texture analysis in the context of tumor imaging (1), assuming that textural features could reflect intratumor heterogeneity, which is known to have important implications in cancer research (2). Texture analysis is also a key component of radiomics (3). Despite promising results, texture analysis has not yet been transferred to the clinic for several reasons, including a limited understanding of the biological meaning of the measured textural features, the lack of evidence of significant added value of textural features compared with more conventional indices in prospective studies, and the insufficient control of the false discovery rates (4). In addition, although various research software programs that enable the calculation of radiomic features (RF) have been developed (examples in Supplementary Table S1), easy-to-install and user-friendly software that can be easily interfaced with the Picture Archiving and Communication System is not yet widely available. Finally, the use of RF in the clinic is hampered by the unavailability of widely validated radiomic models. The identification of robust radiomic models is complicated by the variability of feature values as a function of the acquisition device and acquisition protocols (5–8), although harmonization methods have recently been described (9).

In an effort to boost the promising research regarding the potential and use of textural analysis in medical imaging, we developed freeware dedicated to the easy calculation of RF from medical images that does not require any specific programming skills. The goal was to contribute to reproducible research (10) by offering the scientific and medical community a free and user-friendly way to access parameters that are considered as potential relevant biomarkers so that results from many investigators can be obtained and the role that textural analysis can play in image interpretation and radiomics can be clarified.

Here, we present the main characteristics of the software and two cases in which it was used. The free software was released in February 2016 and has already gathered more than 800 registered users around the world. The software comes with various resources (detailed documentation, video tutorials, and

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Note: Supplementary data for this article are available at Cancer Research Online (http://cancerres.aacrjournals.org/).

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list of bibliographic references) that are all available from www.lifexsoft.org.

Overall Features of the LIFEx Software

LIFEx is a free Java application that does not rely on any commercial library and is implemented for Windows, Linux, and Mac operating systems. Its installation is straightforward from the provided installation packages. Personalized user support is provided.

Elementary functionalities of LIFEx include the following:

- A graphical user interface (GUI) that is similar to the interface offered by scanner vendors. The GUI supports keyboard shortcuts and mouse-driven operations and includes two main panels dedicated to the management of image series and volumes of interest (VOI; Fig. 1).
- A browser for reading DICOM images locally or over a DICOM network from DICOM nodes. Non-DICOM formats (NIFTI-1, JPG, TIFF, PNG, and BMP) are also supported.
- A viewer supporting the synchronized display of coronal, sagittal and transaxial slices, the management of different image layers corresponding to different image series (for instance, PET and CT, or PET and MR, or T1 weighted MR and T2 weighted MR) and maximum intensity projection display. Mouse-driven navigation through an image volume in 3 directions simultaneously is available. Time series can be displayed either as a set of images on a single screen or as a stack of images through which the user can navigate using the mouse button. The viewer supports interseries or intraseries supervised image registration.
- RF calculation using optimized memory access for sparse textural matrix computation. Parallel thread execution is used to speed up the calculation by taking advantage of the available CPU power.
- Exportation of results in a system file supporting screenshots (PNG format), image-derived values (CSV or XLS formats), PDF booklets including sets of screenshots selected by the user, transformation matrix when image registration is performed (TXT), and VOI (NIFTI-1 format).

RF Calculations

In LIFEx, a so-called protocol is a set of elementary functions assembled into a logical workflow to produce a result. LIFEx includes a protocol dedicated to the calculation of RF from medical images with all the necessary tools (Fig. 1).

Segmentation

Three options are available to define the VOI from which RF can be calculated. A VOI drawn using another software and stored as a RTSTRUCT object in a DICOM file or in NIFTI-1 format can be imported. The region can also be drawn manually with the 2D or 3D drawing tool or using a semi-automated segmentation method that operates in a previously drawn loose VOI including the target of interest or in the whole image. The segmentation methods currently offered are threshold-based methods accounting or not for background intensity and a click and draw option that creates a VOI from a seed point defined by the click using a region growing approach.

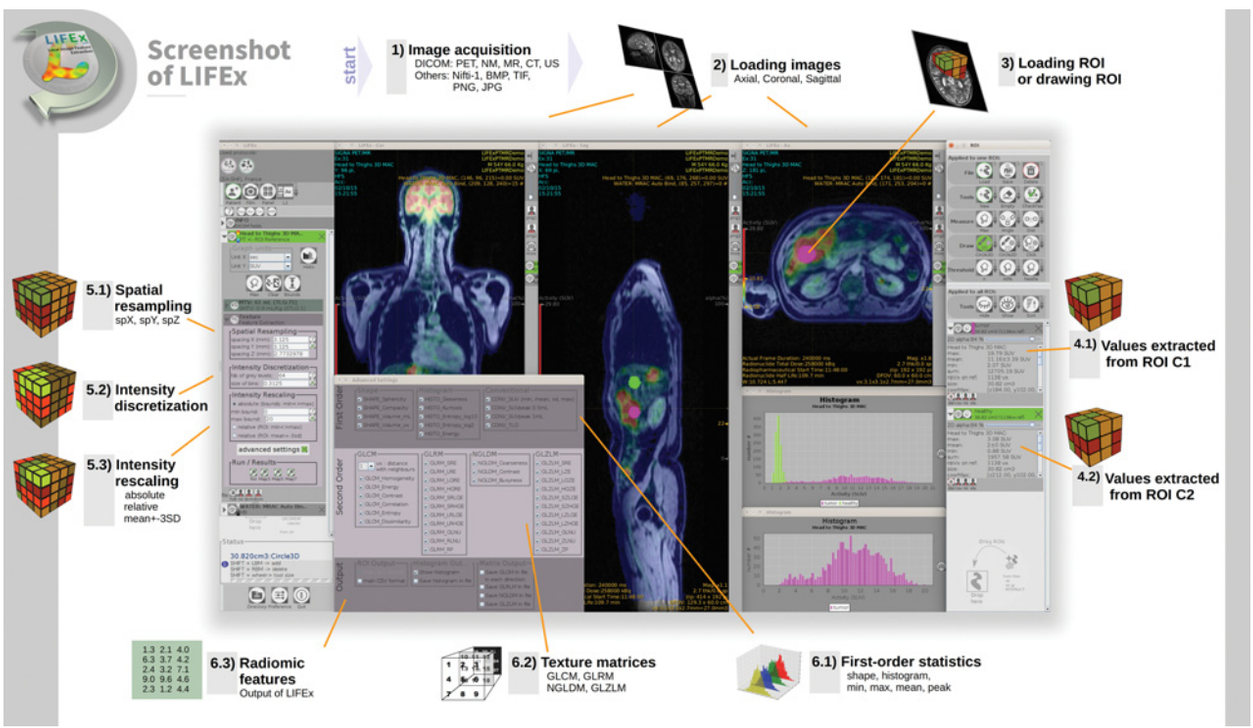

Figure 1.
Snapshot of the LIFEx user interface.

Radiomic index calculation

Some steps involved in the RF calculation significantly affect the results, including the VOI delineation, the quantization of the voxel values before textural index (TI) calculation, the voxel size, and the implementation of textural index calculation in 3D. Voxel value quantization reduces the number of intensity values in the VOI to a fixed set to mitigate the impact of noise on values and to decrease the size of the matrix used for some TI calculations. Relative and absolute quantization is available in LIFEx, yielding significantly different results in terms of tissue-type discrimination and value interpretation (11, 12). Quantization can also be performed in a range defined by the mean and standard deviation voxel values in the VOI. As some TI values depend on the voxel size (13), in LIFEx, the user can specify the voxel size to be used for TI calculation. When the specified voxel size is different from the native one, the image is first resampled to the target voxel size using a Lagrangian polynomial of degree 5. Voxel value quantization is performed after the spatial resampling step if any. In its current version, LIFEx calculates 44 RF reflecting the VOI shape, the VOI voxel values, the histogram of VOI values, or the VOI textural content (see www.lifexsoft.org/index.php/resources/19-texture/radiomic-features for a list of all available RF). TI can be calculated in 2D for 2D regions of interest or in 3D for VOI, where the 3D extension strategy depends on the TI and is fully described in the technical appendix provided with the software (www.lifexsoft.org/index.php/resources/documentation).

LIFEx can be run either interactively or offline using a scripting mechanism. This option is especially relevant when repeated calculations must be performed to explore the impact of some parameters on the results. The script is a simple text file in which successive command lines specify the image filenames to be loaded, the region of interest filename(s) to be read, the settings to be used for the calculations of all radiomic features, and the filename in which the results should be saved. An example of the script is provided (www.lifexsoft.org/index.php/resources/documentation) and can be easily edited to one's own needs.

The integration of LIFEx in a complete radiomic workflow is illustrated in Fig. 2.

Use Cases

Video 1 shows a real-time complete example of radiomic feature calculation from a PET/MR scan where the same VOIs are used to extract PET and MR radiomic features, demonstrating the ease of use of the software. The same process can be applied to any combination of image series and/or parametric image series to obtain a complete multimodality radiomic description of the tumor features.

In a second case study, we show how LIFEx can be used to demonstrate the impact of the voxel size on some RF values in 18F-FDG PET scans of 109 patients with breast cancer (age range = 28–90 years; mean ± 1 SD = 57 ± 15). This study was approved by the institutional ethics committee and the entire patient's data were analyzed retrospectively and anonymously, thus the need for patient approval was waived. Patients were all

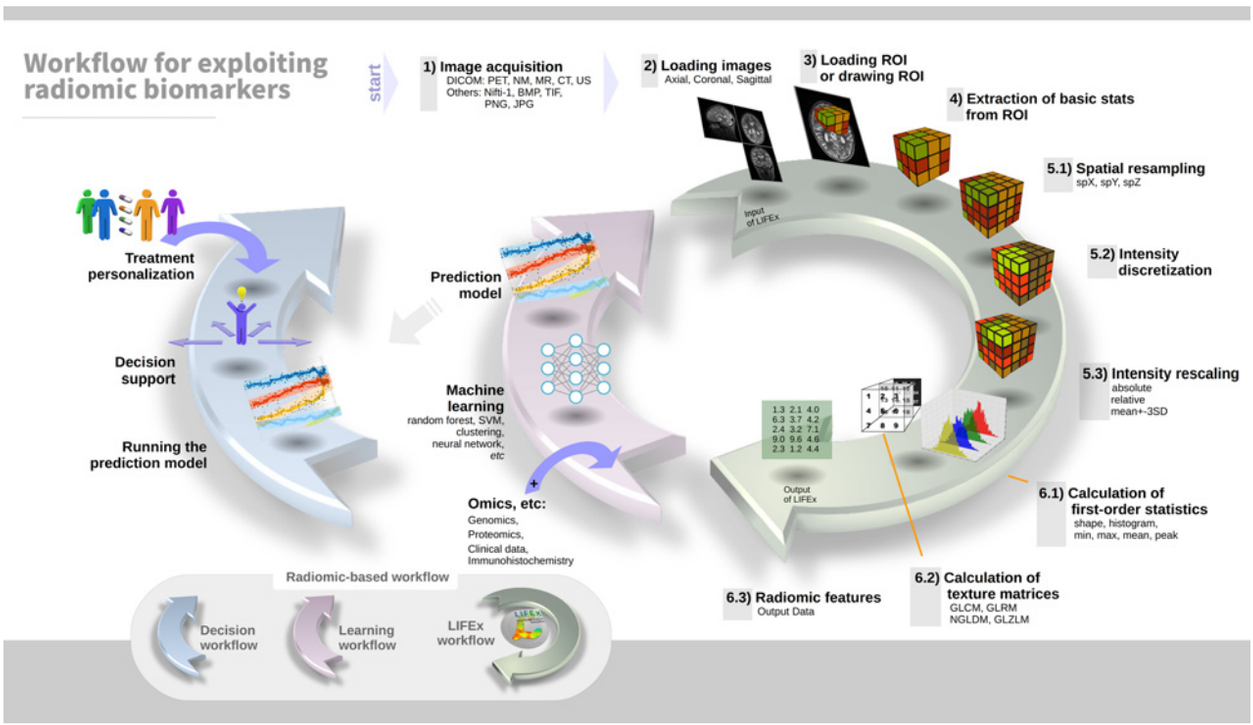

Figure 2.

Workflow of the radiomic processes in which LIFEx can be involved. LIFEx operation (green circular arrow) can be used to calculate radiomic features that are part of the learning workflow (light purple arrow) to derive a radiomic model. LIFEx can also be used to produce the radiomic features entering a radiomic model for decision support (decision workflow, blue arrow).

scanned on a Philips Gemini TF PET/CT scanner, 83 ± 10 minutes (range = 64–108 minutes) after the injection of 18F-FDG (3 MBq/kg). PET images were obtained with 1.45 minutes per bed position and reconstructed using a list-mode iterative algorithm (Blob-Ordered-Subsets-Time-Of-Flight, 2 iterations, 33 subsets). For each patient, five volumes of interest (23 mL in volume each) were drawn in healthy regions, namely, the liver, spleen, lung, muscle, and fatty tissue and in the primary tumor (40% intensity threshold). The RF values were calculated using three different voxel sizes using a script: that of the original images (voxel size = $4 \times 4 \times 4$ mm^3) and $2 \times 2 \times 2$ mm^3 and $1 \times 1 \times 1$ mm^3. Supplementary Fig. S1 clearly shows that some RF values highly depend on the voxel size used for the calculation, unlike the standardized uptake value that is always used in the clinic. These results demonstrate the need to account for voxel size in radiomic model design and application.

Beyond these two examples, LIFEx has been used in a number of publications (www.lifexsoft.org/index.php/resources/publications-journal-papers; www.lifexsoft.org/index.php/resources/publications-conference-abstracts; Supplementary Table S2) with biological and clinical impacts. Images from various PET, CT, MR, and US from different imaging devices (list available from www.lifexsoft.org/index.php/resources/76-list-of-systems-as-lifex-compatible) have been processed. Sample PET/CT, PET/MR and US data are available from www.lifexsoft.org/index.php/resources/data-files for newcomers to try the software.

Discussion

LIFEx has been designed as easy-to-install and user-friendly software enabling RF calculations from medical images and including many options and large flexibility in terms of parameter settings, without the need for any programming skills. By offering it as a free and multi-platform (Mac, Windows, and Linux) tool, the goal is to make radiomic feature calculation accessible to a large community of imaging professionals so that independent and multicenter evidence of the usefulness and limitations of RF for tumor heterogeneity characterization and subsequent patient management can be gathered. LIFEx is an evolving tool (currently V4.00) in which new functions are constantly added as texture analysis and radiomics develop. Feedback from users and interactions with the radiomic community are part of the development strategy.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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