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Automated Lung Nodule Detection and Quantitative Feature Extraction for Data Mining and Decision Support

BROWN MS, Singharuksa S, Lo P, Dubinett S and Aberle DR

Objectives: To evaluate a computer-aided (CAD) system to automatically detect, segment, and extract image features from lung nodules for classification.

Materials/Methods: To evaluate the system it was used in a cohort of 48 subjects to classify nodules pre-surgery into cases with recurrence or death vs no-recurrence at 2.5 years post resection. The automated CAD output was reviewed visually to exclude false positives and to optionally edit nodule segmentations. Quantitative features included nodule size, density, shape, surface, and texture. Two classifiers were machine-learned and compared: (1) using features from the fully automated segmentation; (2) using the semi-automated segmentation, i.e., after manual editing. Classification was performed using logistic regression, retaining only the top 3 discriminative features. Classifier training and testing was performed using cross validation.

Results: 43 of 48 nodules (90%) were detected automatically and 31 of 43 did not require manual editing (72%). There was an average of 1.0 false positives per subject. The weighted classifier accuracy was 77% using the fully automated segmentation of all nodules and 80% after manual editing.

Conclusions: An automated CAD system can reliably extract quantitative imaging features from lung nodules. Manual editing of nodule contours may not be necessary as this only slightly improved classification.

Clinical Relevance/Application: CAD technology can enable quantitative decision support in lung cancer screening. This application aims to better select patients for surgical resection based on quantitative nodule features.

Performance of Maximum Intensity Projection (MIP) and Computer-Aided-Detection (CAD) as Stand-alone Devices in Lung Cancer Screening at Different CT-Dose Levels and Reconstruction Kernels

CHRISTE A, Huber A, Roos JE and Ebner L

Objectives: Evaluate the influence of standard-dose and micro-dose chest CT and three different reconstruction kernels (i30, i50, i70) on the nodule detection rate of two different CAD-systems and the maximum intensity projections (MIP).

Materials/Methods: A total of 226 lung nodules (5, 8, 10, 12 mm, 113 solid and 113 ground glass nodules) were randomly distributed into 55 anthropomorphic lung phantoms. All scans were performed on a 128-row multi-detector CT scanner (Somatom Definition Flash, Siemens, Germany) with a standard dose (100 kVp/100 ref.-mAs) and a microdose level (80 kVp, 6 mAs). The nodule sensitivity of two CAD-softwares (Siemens sygoCT-CAD and Philips Intelli-Space CAD) and two radiologists reading MIP-images (8mm slab / 2 mm slice-thickness) was calculated for standard- and microdose-CT for three different edge enhancing image reconstruction kernels (I30, I50, I70).

Results: The MIP-sensitivity at standard dose level was 97% for all 3 kernels. At microdose level sensitivity for I30, I50 and I70 was 97.6%, 95% and 85.1% (each loss of sensitivity was significant p<0.05). SygoCT-CAD at standard dose reached sensitivities of 96.5%, 97.3% and 96% and dropped at microdose level to 96%, 95.6% and 88.9%. Intelli-Space CAD detected significantly less nodules in all dose/kernel combination, best performance of 73.9% and 69% was reached at I70 for standard and I30 for microdose CT.

Conclusions: MIP can detect as much nodules as a CAD at standard and microdose levels, as long as a soft kernel is used. CAD at microdose-CT works best with softer reconstruction kernels.

Clinical Relevance: MIP as stand-alone device is sufficient compared to CAD for lung cancer screening at microdose levels, but the use of a soft reconstruction kernel (I30) is mandatory.
Lung Cancer Screening with Microdose-CT Imaging Features at Different Reconstruction Kernels

CHRISTE A, Huber A, Roos JE and Ebner L

Objectives: Find the ideal reconstruction kernel for microdose-CT for highest nodule sensitivity, best subjective and objective image quality and lowest nodule diameter measurement error.

Material/Methods: 45 nodules (5, 8, 10 and 12mm) were randomly distributed into 20 anthropomorphic lung phantoms: Micro-dose-CT was performed on a 128-row Somatom Definition Flash (80kVp, 6mAs, 1mm slices, IR) using varying edge enhancing image reconstruction kernels (I30, I50, I70). Nodule sensitivity and interobserver agreement was calculated for 3 readers and a CAD system (syngoCT-CAD). The readers determined subjective image quality (1 to 5), contrast to noise ratio and the axial nodule size. Logistic regression was calculated for all variables.

Results: Mean readers’ sensitivities for I30, I50, I70 kernels were 91.1%±2.2%, 88.9%±4.4% 85.6%±5.6%, where I30 was significantly superior to I70 (p=0.041). CAD sensitivity for I30, I50, I70 kernels reached 95.0%, 99.1%, 90.1%, where I50 was significantly superior to I70 (p=0.004). Lowest nodule measurement error was determined for I30 (-0.212±0.53mm, p-value=0.011). Soft reconstruction kernel (I30) scored the best contrast to noise ratio, subjective image quality and inter-observer agreement. Logistic regression (for sensitivity) = -0.78*(central location)+1.4*(nodule-size>8mm)+1.9*(Reader 1 or 2)-0.89*(Kernel I30 vs. I70) led to significant odds ratios for nodule size and readers of 4.25 (CI 1.04 to 18.o) and 6.97 (95% CI 0.8 to 63).

Conclusions: In a microdose-CT setting I30 or I50 reconstruction kernels allow for best nodule detection with the human eye or the CAD, respectively.

Clinical Relevance: The selection of the correct reconstruction kernel in lung cancer screening has a significant impact on nodule sensitivity.

Computed Tomography Radiation Dose Correlated with Body Mass Index in a Community Lung Cancer Screening Program

DROSTEN R, Hatfield B, Ipsen T, Boga M, and Kuo E

Objective: The goal of this study is to show that low-dose computed tomography (LDCT) scans can be used safely as a screening method for the early detection of lung cancer. We present radiation doses based on body mass index (BMI) in 466 patients screened with LDCT at a community hospital.

Materials and Methods: We scanned 466 patients in Phoenix between 9/11 and 8/14. CT dose length product was recorded. From this value we calculated the effective dose in mSv administered to each patient and subsequently stratified that figure to patients’ BMI. BMI is measured in kg/m2 and is categorized as underweight (<18.5 kg/m2), normal weight (18.5-24.9kg/m2), overweight (25.0-29.9 kg/m2), and obese (≥30 kg/m2).

Results: On average, a non-contrast CT scan exposes a patient to between 6 and 10 mSv of radiation. In our study, the mean radiation dose for all patients was 2.04 mSv (median 2.17 mSv). Effective doses were then stratified based on BMI groups. Underweight patients (2.67%) received a mean radiation dose of 0.93 mSv, normal weight patients (28.57%) received 1.04 mSv, overweight patients (39.3%) received 2.19 mSv, and obese patients (29.46%) received 2.23 mSv.

Conclusion: Lung cancer screening can be performed in a community setting with radiation doses comparable to those obtained in academic institutions as part of the National Lung Cancer Screening Trial. Patients with higher BMIs require greater radiation doses and the risks of screening in this cohort should be further evaluated.

Clinical Relevance/Application: Community lung cancer screening programs can effectively provide LDCT scans of low radiation doses to patients with low and normal BMIs.
CT Lung Cancer Screening: Baseline Results from a Large Italian Screening Program Compared to the NLST Data

OCCHIPINTI M, Franchi P, Tonetti L, Ciliberto M and Bonomo L

Objective: To analyze results from baseline screening in a large Italian screening program and to benchmark these results against those generated by NLST.

Materials and Methods: In a university teaching hospital in a large Italian urban area we enrolled 272 eligible participants at high risk for lung cancer (55 to 74 years old, ≥ 30 smoking pack-years) from September, 2013 to October, 2014. Our program provides yearly screening CTs over 3 years. According to NCCN guidelines, positive nodules were those ≥ 6mm if solid or > 5mm if subsolid. Positive and negative nodule frequencies were determined, and 2 tests were used to compare proportions, both within our program, and between our program and NLST data.

Results: 57/272 participants (20.9%) had a positive result that required a follow-up CT scan in 48 cases and a PET/CT scan in 9 cases. 3/9 (33.3%) PET/CT scans were eventually reported as positive and these patients underwent surgery, confirming adenocarcinoma. So, lung cancer was found in 3/272 participants (1.1%), and all cases were stage I lung cancers. This compares to 27.3% of positive result and to 1% of detected lung cancers in the NLST. Differences between these proportions in the 2 programs were statistically significant for detection of positive results (p=0.02) and not significant for detection of lung cancer (p=0.9).

Conclusions: Results of baseline screening round are equal to those reported by NLST for lung cancer diagnosis. Our statistically significant reduction in rate of positive results can be explained by the higher cut-off for positive results.

Clinical Relevance: Our findings suggest that baseline screening results may be comparable between US and European programs. Definition of positive result is fundamental to reduce unnecessary diagnostic workup and to maximize diagnosis and treatment.

Lung Cancer Screening: Our Low-Dose CT (LDCT) Free Screening Program Experience

PARKER MS, Groves RC, Fahrner LJ, Maldonado M and Bajaj GS

Objectives: To share key elements and results of our free screening program launched during National Lung Cancer Awareness Month, November 2013.

Material and Methods: Our multidisciplinary team determined eligibility based on National Comprehensive Cancer Network (NCCN) type 1 or 2 criteria. Primary Care Practices were notified via letters, e-mail, Internet, posters, and site visits. Educational pamphlets and packets were provided. Communities were informed via mailings, newspaper, radio, TV and billboards. Screens were read within 24 hours and results conveyed to providers and stored in our REDCAP database. LDCT screens were read by thoracic radiologists and reported via the Lahey Clinic LungRADS system.

Results: 400 persons were screened for eligibility. 147 qualified, 77 women and 70 men 53-79 years (mean 61-years). 85 were current and 62 past smokers. 37 desired smoking cessation counseling. Total pack years ranged from 20-106 (mean 45-years). 105 persons met NCCN 1 and 42 met NCCN 2 criteria. Most people learned of the free screens via newspaper (29%) radio (25%) and healthcare providers (24%). Initial LungRADS scores were as follows: 1- 84; 2-2; 3-9; 3i-15; 3n-34; 4-3. On follow-up; 1 LungRADS 3 was upgraded to LungRADS 4. The LungRADS 4 cases included: endobronchial carcinoid (1); poorly differentiated squamous cell (1); poorly differentiated tubular papillary adenocarcinoma (2). All lesions were resected. 66 persons returned a 1-5 point satisfaction survey (mean rating of 4.98).

Conclusion: Our program is a successful model for other institutions.

Clinical Relevance/Application: Our LDCT free screening program experience resulted in 400 potential screens, 147 LDCT eligible patients, and diagnosis and successful treatment of 4 otherwise unsuspected lung tumors.
“Right Dose” Imaging: Iterative Reconstruction CT for Detection of Groundglass and Subsolid Pulmonary Nodules

RICHARDS JC, Schroeder JD, McGehee H, Chung JH, Fuld M and Lynch DA

Objective: To prospectively assess the detection of groundglass and subsolid pulmonary nodules on ultra reduced dose chest CT with sinogram-affirmed iterative reconstruction, with the goal of determining the minimum dose for visual detection of groundglass nodules.

Materials/Methods: Eight subjects have been recruited to date using an institutional lung nodule registry. Nodules were scanned using the routine reduced dose protocol, using automatic exposure control, with filtered back projection of 45 reference mAs (rmAs), then with repeat lower dose scans (20 rmAs and 10 rmAs). The 20 and 10 rmAs scans were reconstructed with three noise-reduction strengths (SAFIRE) [Siemens, Inc], producing a total of 7 series per subject. Images were presented randomly in blinded fashion to a thoracic radiologist who recorded the presence or absence of groundglass nodules on each image and measured the diameter of visualized nodules.

Results: The radiologist reviewer correctly identified each groundglass nodule on all scan series at all doses and with all noise reduction strengths (100% sensitivity). There was no significant difference in nodule measurements between series. A false positive detection occurred in one subject at the lowest dose with all noise reduction strengths.

Conclusions: Reduced dose chest CT with iterative reconstruction protocols at 20 rmAs and 10 rmAs can be used for detection of groundglass nodules at followup chest CT.

Clinical Relevance/Application: With a targeted recruitment of 100 subjects, we hope to show that lower dose protocols with iterative reconstruction and automatic exposure control will optimize detection and measurement of ground glass nodules.

NSCLC with EGFR and KRAS positive genes mutations. The importance of and distinguishing features to differentiate them from other forms of NSCLC

SABRI A, Batool M, Bethune D, Xu Z and Manos D

Purpose: To study the imaging characteristics of lung cancers with EGFR and KRAS mutation compared to other forms of NSCLC.

Methods and Material: Molecular profiling for lung cancer has been performed at our institution since 2012. We performed a retrospective blinded review of Computed Tomography (CT) features for 105 profiled tumors in patients who consented to inclusion in a database.

Results: 15 had KRAS mutation (14%) and 7 with EGFR mutation (7%). Mutation was more common in females than males. 43% of patients with EGFR mutation were smokers compared to 88% in the control group. KRAS positive cancers were more likely to be ground glass or part solid (48% of tumors) compared to KRAS positive (27%) and control group (15%) tumors. Spiculated margin was seen in 29% of EGFR positive tumors, 60% of KRAS positive tumors and 66% of control tumors. Air bronchogram was present in 71% of EGFR positive tumors versus 27% in other groups. The mean doubling time for EGFR positive tumors was 488 days while the doubling time for control group was 255 days.

Conclusion: CT features including tumor size and density on initial CT, doubling time, spiculated margin and presence of air bronchogram may help distinguish subtypes of adenocarcinoma. Further studies should be performed to determine if CT features can be used to identify patients most likely to benefit from molecular profiling.
Using Semantic Features to Distinguish Benign Nodules from Lung Cancer in the Setting of the Indeterminate Nodule in Ever Smokers

SINGHARUKSA S, Kim GH, Oh A, Hsu W and Aberle D

Purpose: To determine the predictive value of semantic(visual) features of nodules in distinguishing benign disease from lung cancers.

Material and Methods: Consecutive chest CT interpretations in 2004-2011, were retrieved from our system. Reports were reviewed if patients were 55-80 years old, ever smokers, and no active cancer within two years. Reports identified nodule 6-25 mm longest diameter on CT images of 1 mm slice thickness. One radiologist analyzed features included longest diameter, anatomic location, consistency, margin, peri-nodule and global lung features. Multivariate logistic regression model determined features that best discriminate benign from malignant. Final classifier was computed as area under the curve (AUC). Bootstrapping checked robustness of factors. Our institutional review board approved this retrospective study.

Results: There were 89 nodules in 89 patients. Cohort included 46 (51.7%) males and 43 (48.3%) females with a median age 67.7 year (SD = 6.1). There were 32 (36%) malignant and 57 (64%) benign nodules. Mean size of nodules was 12.7 mm (SD = 5.5). Anatomic location, margin, present vascular convergence, and size were individually significant features in discriminating benign from malignant (all p < 0.05). In multivariate logistic regression, the most robust features were margin (smooth vs. non-smooth) and increasing nodule size (AUC = 0.85). Neither age nor sex was significant in the predictive model.

Conclusion: Semantic features can predict malignant nature of indeterminate nodules. Nodule margins, size, anatomic location and present vascular convergence were most discriminating.

Clinical Relevance/Application: Semantic analysis can be helpful in predicting the benign or malignant nature of indeterminate nodules in ever smokers.