SSK11

Molecular Imaging (Oncology)

Wednesday, Nov. 30 10:30AM - 12:00PM Room: S504CD

MI RO

AMA PRA Category 1 Credits ™: 1.50
ARRT Category A+ Credits: 1.50

FDA Discussions may include off-label uses.

Umar Mahmood, MD, PhD, Charlestown, MA (*Moderator*) Research Grant, Sabik Medical Inc; Advisory Board, Blue Earth Diagnostics Ltd;
Yasuhisa Fujibayashi, PhD, Fukui, Japan (*Moderator*) Nothing to Disclose

Sub-Events

SSK11-01 A Dual-Labeled Anti-CD 146 Monoclonal Antibody for PET/NIRF Detection of Liver Malignancies

Awards
Student Travel Stipend Award

Emily B. Ehlerding, Madison, WI (*Presenter*) Nothing to Disclose
Reinier Hernandez, MSc, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Haiyan Sun, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Yunan Yang, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Christopher England, PhD, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Todd Barnhart, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Weibo Cai, PhD, Palo Alto, CA (*Abstract Co-Author*) Nothing to Disclose

PURPOSE

Due to hepatic clearance of the majority of contrast agents, molecular imaging of liver malignancies is challenging. However, overexpression of CD146 has been associated with aggressiveness and metastatic potential in liver cancer. Herein we develop a CD146-targeted probe for high contrast positron emission tomography (PET) and nearinfared fluorescence (NIRF) imaging of liver cancer.

METHOD AND MATERIALS

In vitro expression levels of CD146 were characterized in the liver cancer cell lines HepG2 (+) and Huh7 (-) via several in situ methods. YY146, an anti-CD146 monoclonal antibody, was conjugated to the NIRF dye ZW800-1 and to deferoxamine (Df) for radiolabeling with 89Zr. Sequential PET and NIRF imaging were performed after intravenous injection of 3.7 – 7.4 MBq of 89Zr-Df-YY146-ZW800 in athymic nude mice bearing HepG2 or Huh7 subcutaneous (s.c.) xenografts. Orthotopic tumors were generated by injection of luciferase-transfected HepG2 cells into the liver, allowing progression monitoring by bioluminescent imaging. Multimodality imaging was carried out in mice with confirmed orthotopic liver tumors as described for s.c. tumors. At 168 h p.i., tissues were collected for ex vivo NIRF imaging, biodistribution, and histological studies.

RESULTS

PET and NIRF imaging unveiled a prominent and persistent uptake of 89Zr-Df-YY146-ZW800 in HepG2 tumors that peaked at 31.7±7.2 %ID/g 72 h p.i. Owing to such marked accumulation, the detection of orthotopic HepG2 tumors was successful despite the relatively high liver background. CD146-negative Huh7 and CD146-blocked HepG2 tumors exhibited significantly lower 89Zr-Df-YY146-ZW800 accretion (6.1±0.5 and 8.1±1.0 %ID/g at 72 h p.i., respectively), demonstrating the CD146-specificity of the tracer in vivo. Ex vivo studies verified the accuracy of the imaging data and correlated 89Zr-Df-YY146-ZW800 uptake with in situ CD146 expression.

CONCLUSION

Overall, 89Zr-Df-YY146-ZW800 showed excellent properties as a PET/NIRF imaging agent, including high specificity for CD146-expressing liver cancer. Molecular imaging using dual-labeled YY146 had great potential for noninvasive detection and image-guided resection of liver malignancies.

CLINICAL RELEVANCE/APPLICATION

Liver malignancies are often difficult to distinguish from background tissue. Thus, we present a dual nearinfared- and radio-labeled antibody targeting CD146 for detection of these malignancies.

SSK11-02 Role of 11C-Acetate and 18F FDG Dual Tracer PET-CT Scan for Detection of Hepatocellular Carcinoma

Wednesday, Nov. 30 10:40AM - 10:50AM Room: S504CD

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Pek Lan Khong, MBBS, FRCR, Hong Kong, Hong Kong (*Abstract Co-Author*) Nothing to Disclose
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PURPOSE

Up to 45% of Hepatocellular Carcinoma (HCC) show atypical contrast enhancement (CE) pattern on CT/MR, thereby requiring

histologic confirmation. The aim of this study is to evaluate the additional value of Dual Tracer (DT) PET with 11C Acetate (Ac) and 18F FDG for detection and characterization of HCC.

METHOD AND MATERIALS

Consecutive patients who had histological confirmation of HCC and underwent CT/MR and DT in our centres from 2014-16 were identified. CE and PET uptake patterns were reviewed. Typical CE pattern on CT/MR was arterial hyperenhancement followed by portovenous/delayed phase washout. All other CE patterns were considered atypical. On PET, a lesion was deemed positive by visual inspection of lesion above background liver uptake on Ac and/or FDG. Results were compared with tumor size and grade on histology. Tumour size were separated into <3 cm, 3-5 cm and >5 cm groups as each has different treatment option. Grading was based on Edmondson and Steiner system. Pearson's Chi-Square tests were applied to compare the sensitivities and ANOVA-test for subgroup analysis.

RESULTS

Thirty-two HCC lesions from 24 patients were identified (mean size ± SD 34 ± 27 mm). The sensitivity of CT/MR by CE pattern was 53%, FDG alone 56%, Ac alone 94%, DT 97% and combined CT/MR with DT 100% ($p<0.0001$).Two lesions were non-Ac avid. Enhancement pattern were not affected by tumour size whereas FDG sensitivities increase with tumour size from 39% to 67% and 75% for lesions <3 cm, 3-5 cm and >5cm respectively.Histological grade available in 30 lesions were well differentiated HCC (n=7), moderately-differentiated HCC (n=22) and poorly differentiated HCC (n=1). Atypical enhancement pattern was more common in well-differentiated compared to moderately-differentiated lesions (71% vs 45%). No trend was observed for tracer avidities in different grades of HCC.

CONCLUSION

DT combined with CT/MR increases the sensitivity of HCC detection compared to CT/MR alone, providing 100% sensitivity and hence, being most helpful in equivocal liver lesions with atypical contrast enhancement.

CLINICAL RELEVANCE/APPLICATION

The use of DT obviates tissue sampling for diagnosing HCC in patients with liver lesions with atypical CT/MR contrast enhancement.

SSK11-03 64Cu-Labeled Ipilimumab for Determination of CTLA-4 Levels in Lung Cancer

Wednesday, Nov. 30 10:50AM - 11:00AM Room: S504CD

Emily B. Ehlerding, Madison, WI (*Presenter*) Nothing to Disclose
Christopher England, PhD, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Stephen Graves, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Glenn Liu, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Robert J. Nickles, PhD, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Weibo Cai, PhD, Palo Alto, CA (*Abstract Co-Author*) Nothing to Disclose

PURPOSE

CTLA-4 is expressed on the surface of activated T cells and some cancer cells, and is the target of the clinically-approved monoclonal antibody Ipilimumab. Ipilimumab is only successful in a small subset of patients, making neoadjuvant patient selection crucial. In this study, we employ radiolabeled 64Cu-DOTA-Ipilimumab to monitor CTLA-4 expression levels in subcutaneous (s.c.) lung cancer xenografts using positron emission tomography (PET).

METHOD AND MATERIALS

Ipilimumab was conjugated with the chelator 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) for radiolabeling with 64Cu ($t_{1/2}$ = 12.7 h). Western blot, ELISA, flow cytometry, and live cell imaging were employed to determine the CTLA-4 expression levels of three lung cancer cell lines: A549, H460, and H358. Longitudinal PET studies following intravenous injection of 64Cu-DOTA-Ipilimumab into mice bearing s.c. xenografts of the aforementioned lung cancer cells allowed for tracer uptake to be quantified up to 48 h p.i. Ex vivo biodistribution and histological studies were employed to verify PET results.

RESULTS

By in situ analysis, A549 was found to have the highest CTLA-4 expression level, and H358 the lowest. PET quantification verified these results, with A549 tumor uptake peaking at 13.1 ± 3.9 %ID/g, H460 at 10.5 ± 1.9 %ID/g, and H358 at 8.3 ± 1.3 %ID/g, 48 h p.i. A549-blocked mice also displayed decreased tracer uptake values at 8.1 ± 1.0 %ID/g. Ex vivo analysis following the terminal imaging timepoint also corroborated these findings.

CONCLUSION

Radiolabeled 64Cu-DOTA-Ipilimumab is able to differentiate tumors based on their CTLA-4 expression levels noninvasively using PET. Thus, this antibody holds promise to be employed in small doses prior to immunotherapy treatment to predict the success of such anti-CTLA-4 therapy and aid in patient selection.

CLINICAL RELEVANCE/APPLICATION

Anti-CTLA-4 immunotherapies are effective in a small subset of patients. Thus, we use 64Cu-DOTA-Ipilimumab to determine tumors which have high expression levels and may respond well to such therapy.

SSK11-04 Molecular Optical Imaging in Radiofrequency Heating-Enhanced Direct Intratumoral HSV-TK Gene Therapy of Cholangiocarcinoma

Wednesday, Nov. 30 11:00AM - 11:10AM Room: S504CD

Yin Jin, MD, Seattle, WA (*Presenter*) Nothing to Disclose
Feng Zhang, MD, Seattle, WA (*Abstract Co-Author*) Nothing to Disclose
Jun Gao, MD, PhD, Seattle, WA (*Abstract Co-Author*) Nothing to Disclose
Xiaoming Yang, MD, PhD, Seattle, WA (*Abstract Co-Author*) Nothing to Disclose

PURPOSE

To validate the feasibility of using molecular optical imaging to monitor radiofrequency heating (RFH)-enhanced herpes simplex virus

To validate the feasibility of using molecular optical imaging to monitor radiofrequency heating (RFH) enhanced herpes simplex virus thymidine kinase (HSV-TK)/ganciclovir (GCV) therapy of cholangiocarcinomas.

METHOD AND MATERIALS

This study included in-vitro confirmation experiments with luciferase/mCherry-labelled human cholangiocarcinoma cells (Mz-Cha-1) and in-vivo validation experiments using mouse models with luciferase/mCherry-cholangiocarcimonas. Both in-vitro and in-vivo experiments were divided into four groups with treatments of: (i) combination therapy (green fluorescent protein (GFP)/HSV-TK/plasmid gene transfection plus RFH at 42°C,and followed by ganciclovir administration; (ii) gene therapy alone; (iii) RFH alone; and (iv) saline. GFP optical imaging was first performed to detect successful expression of GFP/HSV-TK genes, while bioluminescent optical imaging used to follow up tumor responses to various treatments among different groups, which were correlated with subsequent histologic confirmation.

RESULTS

Of in-vitro experiments, MTS assay demonstrated the lowest cell proliferation in combination therapy compared with three control groups (24.1±7.2% vs 41.6±4.9% vs 72.3±7.9% vs 100%, $p<0.05$). Of in-vivo experiments, GFP optical imaging detected greater green fluorescent signal from GFP/HSV-TK/plasmid-transfected tumors than non-gene transfected tumors (200.73±37.85 VS 52.80±17.36, $p<0.05$), which indicated successful expression of GFP/HSV-TK genes. Bioluminescent optical imaging demonstrated decreases of both bioluminescence signals and tumor sizes in combination therapy, compared to other control groups (0.68±0.11 vs 1.47±0.19 vs 2.01±0.33 vs 2.33±0.41, $p<0.05$), which were confirmed by histologic correlation (Figure).

CONCLUSION

We have established the "proof-of-principle" of using molecular optical imaging to monitor RFH-enhanced GFP/HSV-TK/plasmid gene expression and HSV-TK/GCV gene therapy of cholangiocarcinoma.This concept may pave a new avenue for management of pancreatobiliary malignancies by simultaneous integration of molecular optical imaging, radiofrequency technology, interventional oncology,and direct intratumoral gene therapy.

CLINICAL RELEVANCE/APPLICATION

This concept may pave a new avenue for management of cholangiocarcinoma by simultaneous integration of molecular optical imaging,radiofrequency technology,interventional oncology,and gene therapy.

SSK11-05 89Zr-Labeled Pembrolizumab for Neoadjuvant Imaging and Human Dosimetry Estimation

Wednesday, Nov. 30 11:10AM - 11:20AM Room: S504CD

Emily B. Ehlerding, Madison, WI (*Presenter*) Nothing to Disclose
Christopher England, PhD, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Reinier Hernandez, MSc, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Stephen Graves, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Todd Barnhart, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Weibo Cai, PhD, Palo Alto, CA (*Abstract Co-Author*) Nothing to Disclose

PURPOSE

Pembrolizumab is a clinically-available humanized monoclonal antibody that targets programmed cell death protein (PD-1) on the surface of activated T and B cells. In order to potentially identify patients who would benefit from such therapy, herein we evaluate the pharmacokinetics, biodistribution, and dosimetry of 89Zr-labeled pembrolizumab in vivo using positron emission tomography (PET).

METHOD AND MATERIALS

Pembrolizumab was conjugated with the chelator desferrioxamine (Df) for radiolabeling with 89Zr ($t_{1/2}$ = 3.3 days). Whole-body tracking of the radiolabeled antibody was compared in two murine models, including NSG and PBL mice (NSG mice reconstituted with human peripheral blood mononuclear cells). Mice were injected with 5-10 MBq of radiolabeled antibody. Timepoints from 0.5 h to 168 h p.i. were utilized in the PET study to fully capture the pharmacokinetics of Pembrolizumab. Biodistribution data obtained from PET scans were extrapolated to predict radiation dose estimates in humans.

RESULTS

In all groups, 89Zr-Df-Pembrolizumab stayed in circulation throughout the study and accumulated greatest in liver and spleen. Notable biodistribution differences between PBL and NSG mice included significant uptake in salivary glands in PBL mice, indicating the specificity of Pembrolizumab for human T-cells, which localize here following an autoimmune response. Peak uptake values for the liver of 14.40 ± 1.55 %ID/g for PBL and 12.93 ± 1.96 %ID/g for NSG mice, and for the spleen of 7.33 ± 1.53 %ID/g for PBL and 5.48 ± 0.71 %ID/g for NSG were found 0.5 h p.i. with values steadily declining thereafter. Even with relatively high uptake in these clearance organs, the estimated doses remained well within safe limits, with a total body effective dose of 0.515 ± 0.005 mGy/MBq calculated.

CONCLUSION

The low total body and major organ doses found in this study indicate the potential use of 89Zr-Df-Pembrolizumab for the clinical selection of patients that may benefit from anti-PD-1 therapy. The techniques in this study may be further applied to other antibodies for better understanding of the pharmacokinetics, biodistribution, and dosimetry for future clinical applications.

CLINICAL RELEVANCE/APPLICATION

Herein we evaluate a radiolabeled, clinically-approved antibody, 89Zr-Df-Pembrolizumab, targeting PD-1, that could potentially screen for patients who would respond to such anti-PD-1 immunotherapy.

SSK11-06 Prolactin Receptor-Mediated Internalization of Imaging Agents Detects Epithelial Ovarian Cancer with Enhanced Sensitivity and Specificity

Wednesday, Nov. 30 11:20AM - 11:30AM Room: S504CD

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Yilin Zhang, PhD, Chicago, IL (*Abstract Co-Author*) Nothing to Disclose

Brian B. Roman, PhD, Chicago, IL (*Abstract Co-Author*) Nothing to Disclose
Joseph A. Piccirilli, PhD, Chicago, IL (*Abstract Co-Author*) Nothing to Disclose
Ernst Lengyel, MD,PhD, Chicago, IL (*Abstract Co-Author*) Nothing to Disclose

PURPOSE

To develop a highly sensitive, specific, and clinically amenable molecular imaging agent for ovarian cancer diagnosis that enables (i) detection of tumors when they are still small, confined to the pelvis, and curable and (ii) differentiation between benign and malignant ovarian tumors.

METHOD AND MATERIALS

We used tissue microarray analysis to identify the prolactin receptor (PRLR) as a high specificity biomarker for malignant OvCa. We conjugated gadolinium-chelates and near-infrared fluorescence imaging probes to human placental lactogen (hPL), a specific and high affinity PRLR ligand, and evaluated internalization by PRLR (+) and PRLR (-) ovarian cancer cells. We further evaluated that capacity of hPL-conjugates and reduced binding hPL analog conjugates to imaging mouse xenografts of human ovarian cancer by magnetic resonance imaging and near-infrared fluorescence imaging.

RESULTS

Our results indicate that > 98% of OvCas over-express PRLR regardless of stage, grade, and type. Furthermore, we show both hPL-gadolinium conjugates and hPL-near-infrared probes conjugates internalize specifically and efficiently into PRLR (+) cancer cells in OvCa mouse models. This enables detection of xenograft PRLR (+) tumors in mice with substantially greater specificity and sensitivity than currently used clinical contrast agents.

CONCLUSION

Using prolactin receptor-mediated internalization, hPL-conjugates demonstrate the specificity to distinguish PRLR (+) from PRLR (-) tumors in mouse models of ovarian cancer. Given that > 98% of OvCas over-express PRLR, we believe our ability to image PRLR will enhance specificity and sensitivity of ovarian cancer diagnosis.

CLINICAL RELEVANCE/APPLICATION

Given the difficulties of currently used methods for ovarian cancer diagnosis, we believe molecular PRLR imaging using hPL-conjugates will engender a new paradigm for targeted molecular imaging of OvCa. Coupled with magnetic resonance imaging, molecular PRLR imaging holds the potential to achieve a more precise and earlier diagnosis of OvCa, thereby reducing the number of unnecessary surgeries and increasing patient survival.

SSK11-07 Designed Multifunctional Gold Nanocomposites for Targeted Tri-Mode CT/MR/ Optical Imaging of Human Non-Small Cell Lung Cancer Cells

Wednesday, Nov. 30 11:30AM - 11:40AM Room: S504CD

Jingwen Chen, Shanghai, China (*Presenter*) Nothing to Disclose
Qian Chen, Shanghai, China (*Abstract Co-Author*) Nothing to Disclose
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Han Wang, MD, PhD, Shanghai, China (*Abstract Co-Author*) Nothing to Disclose

PURPOSE

The high incidence and mortality rate of non-small cell lung cancer (NSCLC) prompts exhaustive efforts to develop new effective methods for its diagnosis at the early-stage to improve the survival rate. We are developing multifuctional gold nanocomposites to use as the nanoprobes for targeted tri-mode CT / MR / optical imaging of human non-small cell cancer cells both in vitro and in vivo.

METHOD AND MATERIALS

Amine-terminated generation 5 poly(amidoamine) dendrimers were used as a nanoplatform to be covalently modified with Gd chelator, Cy5.5, and FA. Then the multifunctional dendrimers were used as templates to entrap gold nanoparticles, followed by chelating Gd(III) ions and acetylation of the remaining dendrimer terminal amines.The thus-formed multifunctional Au DENPs (in short, Cy5.5-Gd-Au DENPs-FA) were characterized via different techniques, and then were used for both in vitro and in vivo targeted CT/ MR/ NIR optical tri-mode imaging of human NSCLC cells (NCI-H460 cells) and the xenograft tumor model.

RESULTS

CT/MR/optical images show that NCI-H460 cells can be detected after incubation with the Cy5.5-Gd-Au DENPs-FA in vitro and the xenograft tumor model can be imaged after intravenous administration of the particles. Combine the inductively coupled plasma-atomic emission spectroscopy (ICP-AES) measurements with the transmission electron microscopy (TEM) data confirm that the Cy5.5-Gd-Au DENPs-FA is able to be uptaken by the treated cells. MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay show that the Cy5.5-Gd-Au DENPs-FA has a good biocompatibility at the given concentration range.

CONCLUSION

The findings of this study suggest that the developed Cy5.5-Gd-Au DENPs-FA may be used as a promising tri-mode nanoprobe for targeted CT/MR/opticl imaging of human NSCLC and other folate receptor (FR) over-expressing cancers.

CLINICAL RELEVANCE/APPLICATION

In consideration of the special structural characteristic, the dendrimer based nanocomposites may be further modified with therapeutic antibodies or small interfering RNA (siRNA) to be expectably developed for the personalized theranostics of cancers at early-stage with the high accuracy and sensitivity.

SSK11-08 Differential Uptake of CD146-Specific Antibody in Solid Lung Malignancies

Wednesday, Nov. 30 11:40AM - 11:50AM Room: S504CD

Christopher England, PhD, Madison, WI (*Presenter*) Nothing to Disclose

Haiyan Sun, Da Lian, China (*Abstract Co-Author*) Nothing to Disclose
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Yunan Yang, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Todd Barnhart, Madison, WI (*Abstract Co-Author*) Nothing to Disclose
Weibo Cai, PhD, Palo Alto, CA (*Abstract Co-Author*) Nothing to Disclose

PURPOSE

Recent studies have revealed that a cell surface protein called CD146 is a marker of epithelial-to-mesenchymal transition (EMT) in cancer cells whose overexpression has also been found to correlate with cancer progression, invasion, and metastasis. Additionally, CD146 has low background levels in normal tissue as well as differential expression in metastases and advanced primary tumors, showing its significant potential in cancer therapies. This study evaluates the utilization of YY146, an anti-CD146 monoclonal antibody, for molecular imaging of solid lung malignancies.

METHOD AND MATERIALS

The anti-CD146 antibody (YY146) was conjugated to 1,4,7-triazacyclononane-triacetic acid (NOTA) and radiolabeled with 64Cu. CD146 expression was evaluated in six human lung cancer cell lines (A549, NCI-H358, NCI-H522, HCC4006, H23, and NCI-H460) by flow cytometry and quantitative Western blot studies. The biodistribution and tumor uptake of 64Cu-NOTA-YY146 was assessed by sequential PET imaging in athymic nude mice bearing subcutaneous lung cancer xenografts. The correlation between CD146 expression and tumor uptake of 64Cu-NOTA-YY146 was evaluated by graphical software while ex vivo biodistribution and immunohistochemistry studies were performed to validate the accuracy of PET data and spatial expression of CD146.

RESULTS

Flow cytometry and Western blot studies showed similar findings with H460 and H23 cells highly expressing CD146. Small differences in CD146 expression levels were found between A549, H4006, H522, and H358 cells. Tumor uptake of 64Cu-NOTA-YY146 was highest in CD146-expressing H460 and H23 tumors, peaking at 20.1 ± 2.86 and 11.6 ± 2.34 %ID/g at 48 h post-injection (n=4). Tumor uptake was lowest in the H522 model (4.1 ± 0.98 %ID/g at 48 h post-injection; n=4), while H4006, A549 and H358 exhibited similar uptake of 64Cu-NOTA-YY146. A positive correlation was found between tumor uptake of 64Cu-NOTA-YY146 (%ID/g) and relative CD146 expression ($r2=0.98$, $p<0.01$). Ex vivo biodistribution corroborated the accuracy of PET data.

CONCLUSION

The strong correlation between tumor uptake of 64Cu-NOTA-YY146 and CD146 expression demonstrates the potential use of this radiotracer for imaging tumors that elicit varying levels of CD146.

CLINICAL RELEVANCE/APPLICATION

This imaging tracer may promote enhanced monitoring of therapeutic response and improved patient stratification.

SSK11-09 Smartphone based Diagnostics (D3) Enable Molecular Characterization of Lymphoma in Resource-limited Countries

Wednesday, Nov. 30 11:50AM - 12:00PM Room: S504CD

Awards
Student Travel Stipend Award

Aoife Kilcoyne, MBBCh, Boston, MA (*Presenter*) Nothing to Disclose
Divya Pathania, Boston, MA (*Abstract Co-Author*) Nothing to Disclose
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Hakho Lee, PhD, Boston, MA (*Abstract Co-Author*) Nothing to Disclose
Cesar Castro, Boston, MA (*Abstract Co-Author*) Nothing to Disclose
Ralph Weissleder, MD, PhD, Boston, MA (*Abstract Co-Author*) Investor, T2 Biosystems, Inc

PURPOSE

A major hurdle in cancer therapy is it's timely diagnosis and treatment. This is of particular concern in resource-limited settings. For example, aggressive forms of non-Hodgkins lymphoma are major health concerns in sub-Saharan Africa. A substantial number of cases evade comprehensive evaluation and are not appropriately classified due to the lack of proper tissue specimens, diagnostic reagents and specialists. Although a good proportion of cases are curable even in low and middle income countries, windows of therapuetic opportunity are often missed due to delay in diagnosis. This necessitates the need for a low-cost, rapid and accurate detection technology to expedite the diagnosis of aggressive lymphomas (and other prevalent cancers) in the resource-limited environment.

METHOD AND MATERIALS

We have developed a digital diffraction diagnostic (D3) platform that allows modern smartphones to be used for molecular cancer diagnostics of scant clinical samples (fine needle aspirates). Fine Needle Aspirate (FNA) samples are immunolabeled with microbeads in a microfluidic module and then holographically detected by the smartphone camera.

RESULTS

Diffraction patterns generated by the antibody-microbeads were detected with the smartphone camera using bright-field settings. Digital signal processing was used to reconstruct images to count bead-bound cells. We optimized the assay so that thousands of cells could be analyzed without washing steps in near real-time. The D3 profiling results on lymphoma cell lines demonstrated excellent agreement with those by flow cytometry (gold standard). We further analyzed scant clinical samples (FNAs) from 8 patients. The D3 assay generated readouts within an hour and demonstrated agreement (100%) with standard pathology.

CONCLUSION

The D3 approach of molecular analysis could have far reaching applications. The major advantages are the simplicity of the method, the accuracy and it's ability to be used in resource-limited settings.

CLINICAL RELEVANCE/APPLICATION

Leveraging smartphones as a mobile diagnostic terminal could empower resource-poor communities with complex laboratory tests.

This work addresses the practical diagnostic needs of low and middle income countries and reflects the type of technologies that may gain sustainable traction in such settings.