Demonstration of the Automated Dicentric Chromosome Identifier and Dose Estimator System (ADCI™) in a Cloud-based Online Environment

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Abstract

Background. Interpretation of cytogenetic metaphase images and quantification of exposures remain labour intensive in radiation biodosimetry, despite computer-assisted dicentric chromosome (DC) recognition and strategies to distribute workloads among laboratories. In a moderate- to large-scale medical emergency, specimen volumes could overload available human resources and delay timely reporting of clinically significant overexposures. Once cell images are captured by a computerized-microscope system, the same computer typically performs image analysis, during which time the system is unavailable for accessing additional samples. Outsourcing the analysis to ADCI, which runs on a dedicated high performance computer system, eliminates this bottleneck and significantly increases overall throughput. ADCI processes the captured images to identify DCs, selects images, and quantifies radiation exposure. It can autonomously determine model selection criteria for optimal image quality, construct dose calibration curves, and estimate whole or partial-body radiation dose in test samples with unknown exposures.

Methods. Windows®-based ADCI has been ported to ADCI_Online, a secure web-streaming platform (AppStream 2.0, Amazon Web Services[AWS]) that can be accessed worldwide with local AWS nodes. Operationally, ADCI_Online is indistinguishable from the version that runs on a dedicated, standalone computer. Because the cloud-based system is configured with lower throughput hardware (2 proc. CPU, 3.75Gb RAM) relative to a Desktop computer running Windows®-based ADCI (Intel I7-7th gen 4 proc. CPU, 16 Gb RAM), processing of metaphase cell images is ~3 fold slower on a per sample basis. The online version is streamed with limited access to the file system. User and sample metadata including identifiers are encrypted in transit to an AWS S3 bucket. Security measures include locking of file directories and file contents, type verification of uploaded metaphase image files, and built-in quality control measures to assure data integrity.

Results. Data analyses generated by ADCI_Online were compared to our previously published studies of the same samples (Rad. Prot. Dosimetry 186[1]: 42-47, 2019; Int J Rad Biol. 96[11]: 1492-1503, 2020). Processing of the 0Gy calibration and HS01 test samples obtained from Health Canada identified DCs at a rate of ~16.6 metaphase images/min with ADCI_Online. Previously processed samples (adcisample files) were uploaded to ADCI_Online for other calibration and test samples. Automated image selection model optimization produced identical rankings for the best models on both systems. Calibration curves were generated, and exposures were determined with the dose estimation wizard for 3 different image section models (A_B, A_C, and A_D). Dose estimates of test samples were identical to previously presented results. Partial-body dose estimation of samples with 50% fractional exposures using an associated calibration curve (for image selection model C_B750) also resulted in nearly identical findings in both systems.

Conclusions. ADCI_Online offers a cost-effective, subscription-based service useful for radiation research, proficiency testing, inter-laboratory comparisons, and training. In a research context, the system could provide highly uniform, reproducible assessment in large studies of many individuals, for example exposed to therapeutic radiation. ADCI_Online compute environments originate from a single snapshot which can be cloned any number of times; thus, the system can be rapidly scaled when required. With robust network connectivity in a medical emergency of multiple potentially radiation exposed individuals, throughput and capacity for multiple samples requiring simultaneous processing and dose evaluation can be expanded to seamlessly mitigate any backlog in sample interpretation.

Methods

On-Demand Remote Access to ADCI

ADCI_Online runs exclusively on the cloud-based system and pixels are streamed to the user through a web browser. The Amazon Web Services (AWS) Image Builder tool was utilized to create a "clean" install of ADCI, meaning ADCI was installed but not subsequently executed to examine samples. A full system image, or "snapshot", was generated which is then duplicated on-demand to create a streaming instance when a new streaming session is requested. By default, a streaming instance boots with the AppStream 2.0 hardware configuration "stream.standard.medium" (2 vCPU, 3.75Gb RAM). Sample processing is ~3 fold slower than the recommended desktop computer running ADCI. Although each system running ADCI_Online has less computing power than a high-performance Microsoft Windows® system running ADCI, the cloud-based nature of ADCI_Online allows for rapid expansion of resources as shown in Figure 1. Users may first upload metaphase images to a user-specific cloud-based storage directory before a streaming session is initiated. User interaction with ADCI is outlined in Figure 2.

Data Management

An AWS Simple Storage Service (S3) Bucket is utilized for storage of uploaded metaphase images and ADCI results. Each user is assigned to a unique directory of the S3 Bucket named with the SHA-256 hash of their e-mail address, and access to directories associated with other users is disabled through the use of AWS Identity and Access Management (IAM) Policies. A user can access their user-specific portion of the S3 Bucket outside of a streaming session through the AWS Management Console (AWS website). The S3 bucket is also mounted to the streaming instance to "C:\Users\PhotonUser\My Files\Home Folder". Files are encrypted in transit to and from S3 storage (HTTPS protocol) and server-side encryption is applied to all files in the Bucket (AWS Key Management Service). For security reasons, internet access within the streaming instance is disabled, and files can only be transferred to/from the streaming instance by way of the S3 Bucket.

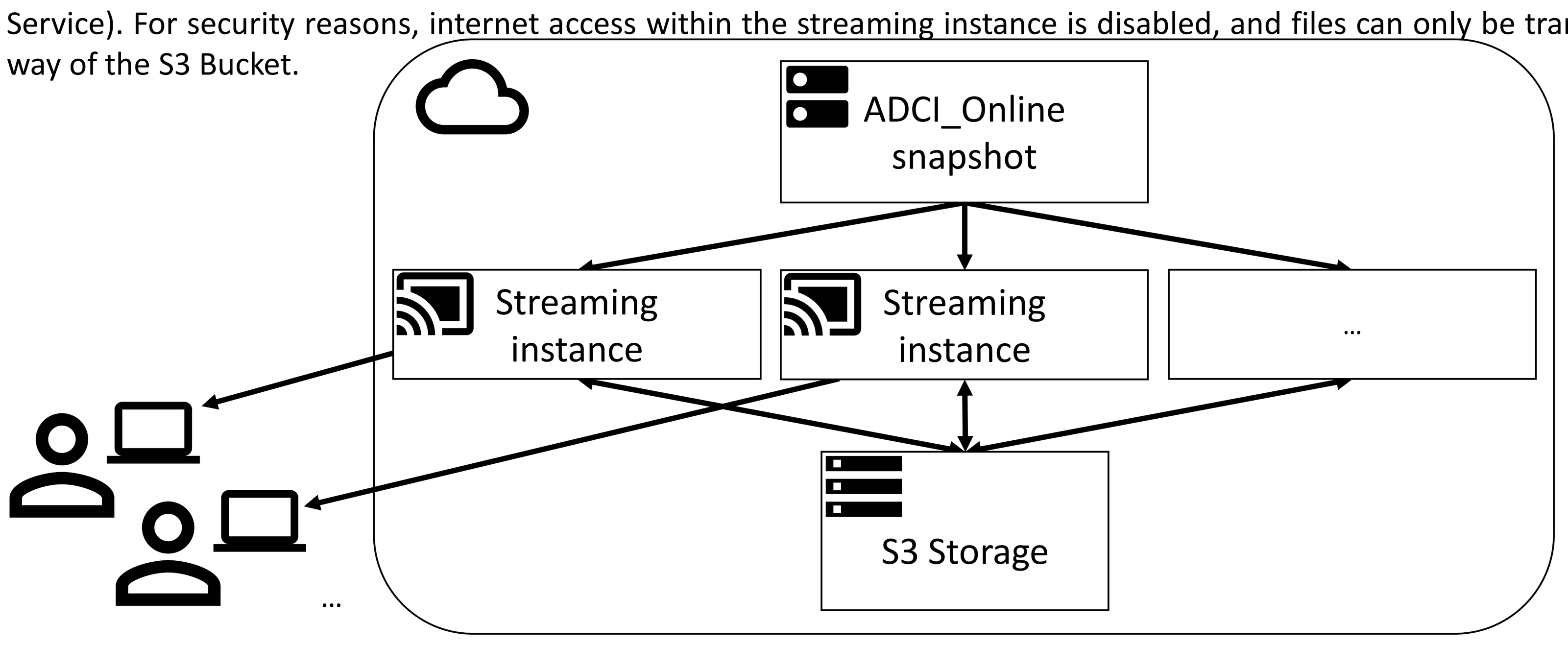

Figure 1. **ADCI_Online leverages a cloud-based environment to expand system resources rapidly on-demand**
When a streaming session is initiated, a new streaming instance is cloned from an existing snapshot of the ADCI_Online system. Thus - when first initiated - all streaming instances are configured identically. Two main possibilities exist to rapidly increase computing resources. The ADCI_Online snapshot may be cloned as many times as necessary, providing an array of cloud-based systems available for use. Another approach is to increase computing resources on each streaming instance. These two options could also be implemented simultaneously.

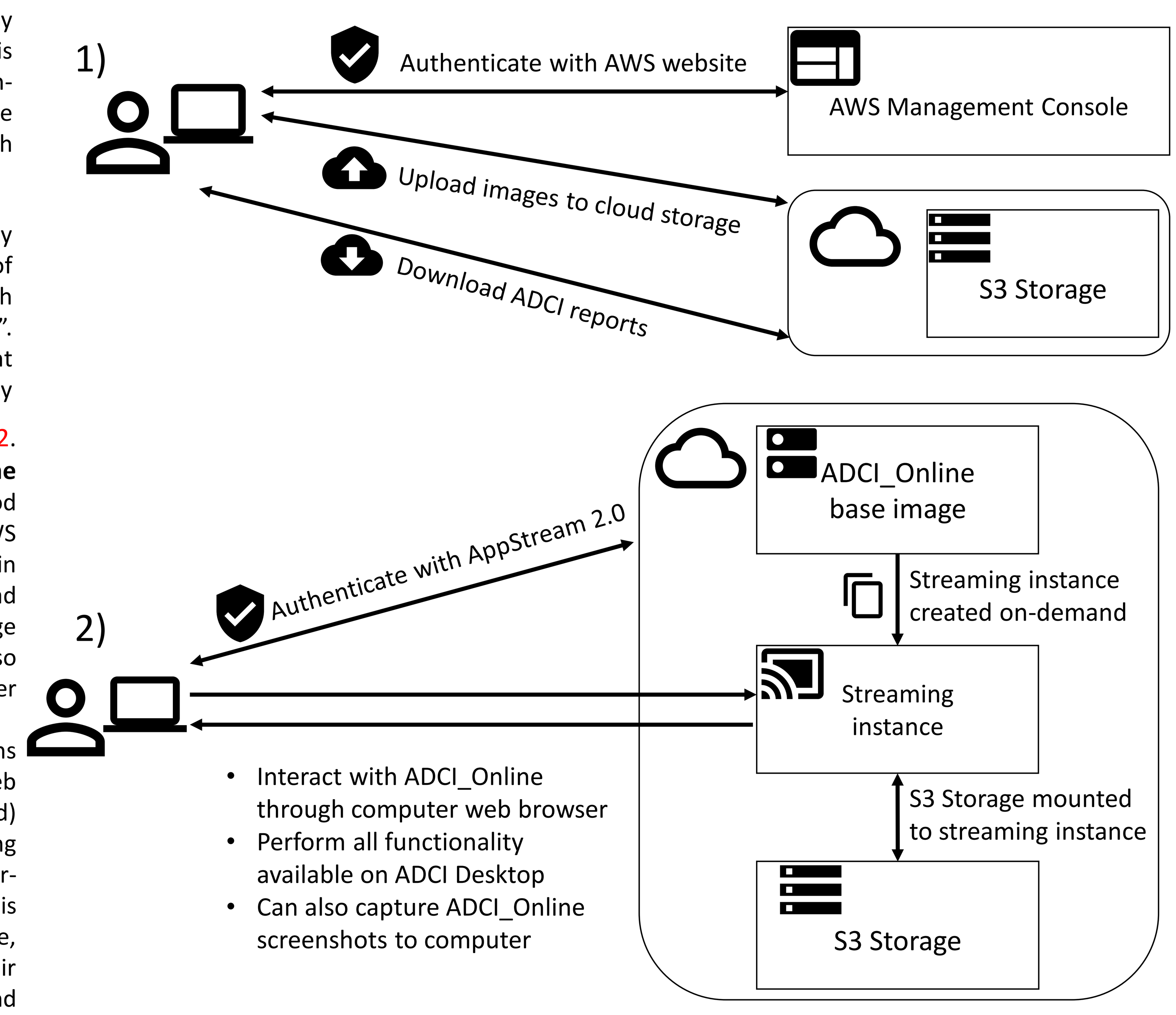

Figure 2.
User interactions with ADCI_Online
1) Before a new subscription period begins, a user may sign into the AWS Management Console (login credentials provided) and upload metaphase images to cloud storage (AWS S3). This mechanism is also used to download ADCI reports after they have been generated.
2) To access ADCI_Online, the user signs into AWS AppStream 2.0 in their web browser (login credentials provided) and requests a new streaming session. Thus, the user-specific S3 storage directory is mounted to the streaming instance, allowing the user to access their uploaded metaphase images and save results generated by ADCI.

Results

Validation of ADCI_Online

Dicentric chromosome counts and dose estimation results obtained through ADCI_Online were compared to those obtained through a standard MS Windows® version of ADCI installed locally. Metaphase images associated with a homogeneously irradiated test sample (HS01) and 2 Gy calibration sample obtained from Health Canada (HC) were uploaded to ADCI_Online and processed. The counts of dicentric chromosomes located by ADCI_Online for these samples matched those obtained locally at all sigma levels. Other previously processed HC and Public Health England (PHE) samples were uploaded to ADCI_Online:

- HC: Dose estimates for homogeneously irradiated samples were generated after application of 4 different image selection models (A_B, A_C, A_D, Automated178981) and matched those previously published results[1].
- PHE: Estimates of partial-body dose and fraction of blood irradiated were generated for partially irradiated samples (PHE_E, PHE_F, PHE_G) and agreed with previously published results[2]. Note slight variation in partial-body results are expected in every analysis due to our false positive removal algorithm for partial-body samples[2] which involves sampling the 0 Gy calibration sample in real-time.

Time Required to Upload Metaphase Images

The HC 2 Gy calibration sample containing 2180 metaphase images (1,772.58 MB on disk) was uploaded to a user-specific S3 Bucket in 1053 seconds, equivalent to a rate of 124.2 images/min. The time required to upload images was excluded from Table 1 as the upload process can occur before an ADCI_Online streaming session begins. However, if a rate of 124.2 images/min is applied to the 16,000 metaphase images examined in Table 1, the time required to upload those images to the S3 Bucket would be 128.8 min. Of course, upload times will vary due to the upload speed offered by the user's internet service provider, among other factors.

Time Required to Process Metaphase Images

The HC 2 Gy calibration sample uploaded to S3 (2180 metaphase images, 1,772.58 MB on disk) was processed on ADCI_Online in 110.89 min, equivalent to a rate of 19.659 images/min. The HS01 test sample (540 metaphase images) was processed in 32.46 min (16.636 images/min). Both samples were processed directly from the mounted S3 Bucket.

Table 1. Estimated Time Required for a Typical ADCI_Online Session

User Action	Time
Process calibration samples	
7500 metaphase images in 7 calibration samples • 3 samples < 1 Gy (1500 images), 4 samples >= 1Gy (750 images) • Assuming image processing rate of 19.659 images/min	6 h, 22 m
Automated image selection model generation	
Evaluation modes: Curve fit residuals or p-value of Poisson fit	1 h, 34 m
Evaluation mode: Leave-one-out	3 h, 53 m
Process test samples	
8500 metaphase images in 10 test samples • 7 homogeneously irradiated samples (700 images), 3 partially irradiated (1200 images) • Assuming image processing rate of 19.659 images/min	7 h, 12 m
Other operations	
Optional - Review of processed samples in metaphase image viewer	variable
Review of image selection models	30 – variable m
Calibration curve generation	5 – 30 m
Dose estimation	5 – 30 m
Report generation and review	10 – 120 m

One-time setup (process calibration samples and automated image selection model generation)
Only one evaluation method necessary (evaluation modes)

Conclusion

- ADCI_Online offers a cost-effective subscription-based service useful for radiation research, proficiency testing, inter-laboratory comparisons, and training.
- Dose estimation can be carried out anywhere there is a reliable internet connection.
- Security of data was considered at every step of the development process, with images and results encrypted and stored in an S3 Bucket directory accessible only to them.
- ADCI_Online can be rapidly scaled to meet "burst" requirements such as individuals in an emergency situation requiring processing of many samples.

External Content

Introduction and access to demonstration version - https://radiation.cytognomix.com
Partnerships and contact e-mail address - info@cytognomix.com
How ADCI works (online manual) - https://adciwiki.cytognomix.com
Dicentric chromosome classification by machine learning - https://cytobiodose.cytognomix.com
ADCI protocol in the Journal of Visualized Experiments (JoVE) - https://doi.org/10.3791/56245
To obtain ADCI - https://radiation.cytognomix.com/quoterequest.php

References

1. Li Y, Shirley BC, Wilkins RC, Norton F, Knoll JHM, Rogan PK (2019). Radiation dose estimation by completely automated interpretation of the dicentric chromosome assay. Rad Prot Dosim. 186:1, 42–47. DOI: 10.1093/rpd/ncy282

2. Shirley BC, Knoll JHM, Moquet J, Ainsbury E, Pham ND, Norton F, Wilkins RC, Rogan PK (2020). Estimating partial-body ionizing radiation exposure by automated cytogenetic biodosimetry. Int J Radiat Biol. 96:11, 1492-1503. DOI: 10.1080/09553002.2020.1820611

Acknowledgements of Support

IAEA
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