The Gulf Journal of Oncology

Indexed By PubMed and Medline Database

Issue 52, Sep 2026
ISSN No. 2078-2101







Under the Patronage and Honoring of HRH Prince Saud bin Nayef bin Abdulaziz, Governor of the Eastern Province: Saudi Cancer Foundation Successfully Launches "AlSharqia Wardiyah 18"

The Official Journal of the Gulf Federation For Cancer Control

Table of Contents

Original Articles:

Clinico–Demographic Variables Affecting Survival in Esophageal Cancer: Real–World Evidence from a Tertiary Cancer Centre in Western India **07**
Samiran Chavan, Atul Kumar Gupta, Bharti Devnani, Puneet Pareek

Characteristics of hospital readmissions within 30 days among adult patients with cancer in Jordan **14**
Nour M. Mustafa, Pharm D, BCOP, Dima Attili, Pharm D, Nour Faqeer, Pharm D, BCOP

Efficacy of Volumetric Modulated Arc Therapy (VMAT) in Nasopharyngeal Carcinoma: A Retrospective Analysis. **20**
Venkada Manickam Gurusamy, Palmira Caparrotti, Hissa Hussain Al–Abdulla, Saju Raveendran Divakar, Ghazia Shaik, Patsey Conway–Murray, Amna Rafi Vora, Muhammad Usman, Rabih Wafiq Hammoud, Noora Al–Hammadi.

Prevalence, Correlates, and Predictors of Depression and Anxiety Among Cancer Patients in the UAE: A Comprehensive Cross–Sectional Study Using the Hospital Anxiety and Depression Scale (HADS) **29**
Manal Ali Buabeid, Ayesha Alqasem, Maitha Salem Althehli, Shamma Ali Alhefeiti, Faryal Iqbal, Amin Abyad, Hassan Jaafar and Humaid O. Al–Shamsi

Induction spatially fractionated GRID radiotherapy (SFGRT) radiotherapy for locally advanced extremity soft tissue sarcoma: Report of 10 years follow up. **44**
Abdullah Alsuhaibani, Mohammed Almahmoud, Mohammed Mohiuddin, Muhammad Memon, Ahmed Nobah, Medhat Elsebaie, Ayman Elshenenawy, Rajive Pant, Mahmoud Shaheen, Majid Alyamani, Hatim Khoja, Tariq Alzaid, Fouad Al Dayal. Ahmed Elashwah

Modeling Cancer Incidence and Mortality in Yemen Using GLOBOCAN 2020 Estimates: An Empirical and Rank–Based Analysis **52**
Gamal Abdul Hamid, Amen Bawazir, Safa A. Shukry, Taher Bin Sumiat, Noureddine Ouerfelli

Establishing the First Four–Dimensional Multipurpose Central Nervous System Tumors Biobank in Saudi Arabia: Project Design, Perspectives, and Preliminary Results **65**
Deema Hussein, Saleh Baeesa, Alazouf Alhowity, Ishaq Khan, Mona Alomari, Hanadi Qashqari, Nawal Madkhali, Reem Alserihi, Mohammed Bangash, Fahad Alghamdi, Awatif Jamal, Mohamad Saka, Torki AlZughaibi, Ghazi Damanhouri, Adeel Chaudhary, Adel Abuzenadah

Review Articles:

Craniospinal Irradiation (CSI) Techniques: A Systematic Review of Comparative Dosimetric Outcomes, Organ–at–Risk Sparing, and Treatment Efficiency **79**
Kesava Ramgopal Adavikolanu, Chandramouli Ramalingam, Soorej Balan Kaliyath, Abhishek Raghava KS, Thirumal M, Nagasai Divya Kari, Pragnahitha Neerudu, Ambedkar Yadala, Ajay Kumar Kondeti

Case Reports:

Tubular Ileal Duplication Associated with Diffuse Polyposis and Metastatic Adenocarcinoma Presenting as Acute Small Bowel Obstruction in an Adult: First Reported Case and Review of the Literature **92**
Aliasgar I Kachwala, Obaid M Alharbi, Rajan Arora.

Tubulolobular Carcinoma of the Breast: First Case Report from Saudi Arabia **98**
Mehad Ahmed, Wafaey Badawy, Samah O. Mohager

Conference Highlights/Scientific Contributions

- **News Notes** **103**
- **Advertisements** **106**
- **Scientific Activities** **107**

Original Article

Establishing the First Four–Dimensional Multipurpose Central Nervous System Tumors Biobank in Saudi Arabia: Project Design, Perspectives, and Preliminary Results

Deema Hussein[1,2], Saleh Baeesa[3,4*], Alazouf Alhowity[1], Ishaq Khan[1,5], Mona Alomari[1], Hanadi Qashqari[1], Nawal Madkhali[1], Reem Alserihi[1,6], Mohammed Bangash[4], Fahad Alghamdi[7], Awatif Jamal[7], Mohamad Saka[1,2], Torki AlZughaibi[1,2], Ghazi Damanhouri[1], Adeel Chaudhary[8], Adel Abuzenadah[1,2,8]

[1.] King Fahd Medical Research Center, King Abdulaziz University, Jeddah 21589, Saudi Arabia.
[2.] Department of Medical Laboratory Sciences, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah 21589, Saudi Arabia.
[3.] Neurosciences Department, King Faisal Specialist Hospital and Research Center, Jeddah, Saudi Arabia.
[4.] Division of Neurosurgery, Faculty of Medicine, King Abdulaziz University, Jeddah 21589, Saudi Arabia.
[5.] MIT Media Laboratory, Massachusetts Institute of Technology, 75 Amherst St., Cambridge, MA 02139, United States.
[6.] College of Health Sciences, Al–Rayan Colleges, 41411 Madinah Al–Munawarah, Saudi Arabia.
[7.] Pathology Department, Faculty of Medicine, King Abdulaziz University, Jeddah 21589, Saudi Arabia.
[8.] Center of Innovation for Personalized Medicine, Department of Medical Laboratory Technology, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah 21589, Saudi Arabia.

Abstract

Introduction: The burden of central nervous system tumors (CNSTs) is a global challenge. Disease–associated biobanks enable the use of collected human tumor cell samples to improve the understanding of disease biology and advance personalized medicine. However, differences in genetic composition can influence drug treatment outcomes; thus, variable samples collected from different genetic populations are necessary. Currently, tumor cell line data derived from CNSTs related to the Middle Eastern genetic pool are rare in the literature. Therefore, we established a CNSTs biobank that focuses on initiating CNSTs research in vitro in Saudi Arabia.

Materials and Methods: A total of 111 fresh CNSTs specimens were collected between February 2013 and December 2020 from patients who were treated at King Abdulaziz University Hospital in Jeddah, Saudi Arabia. The collection procedure, tissue processing, and in vitro primary cell culture initiation procedures are detailed.

Results: The characteristics of patients and samples collected in the biobank showed a female–to–male ratio of 61:39%, a mean age of 39.7 years, and variable tumor types, including low–grade, high–grade malignant, and metastatic brain tumors. The basic characteristics of tumor tissue samples, including tumor volume, composition, hydration, and vascularization, were not defined by their origin. Primary tumor cell lines were established for histopathologically distinct tumor types, and the observed cells exhibited variable morphologies.

Conclusion: We present the first four–dimensional multipurpose CNSTs biobank protocol design in Saudi Arabia, along with our preliminary results. The cohort study encompassed a diverse range of histologically variable CNSTs, including adult and pediatric cases. By establishing this biobank, we intend to foster national and regional collaborations to enhance translational research and targeted medicine for patients with CNSTs. We also encourage researchers to establish similar biobanks in their respective countries.

Keywords: Cancer, biobanks, central nervous system tumors, primary cell lines, Saudi Arabia.

Correspondence: Saleh S. Baeesa, MD, FRCSC* Department of Neurosciences, King Faisal Specialist Hospital and Research Center, Jeddah, Saudi Arabia. Prince Saud Al–Faisal Road, P.O. Box 40047, Jeddah 21499, Kingdom of Saudi Arabia Office: +966 12667 7777, Ext: 65819, Email: sbaeesa@kfshrc.edu.sa, salehbaeesa@gmail.com, X (Twitter): @Saleh_BaeesaMD, ORCID: 0000–0002–3053–7912

Introduction

The World Health Organization (WHO) reported an estimated 9.6 million cancer–related deaths in 2020. [1] Central nervous system tumors (CNSTs) are estimated to be the 5th cancer killer of cancer–related deaths worldwide. In the USA, these tumors were reported to have an average 5–year survival rate of 36% as reported in 2022. [2] In the Middle East, CNSTs are among the top ten most frequent types of cancer. [3]

To understand the biology of CNSTs, patients' tumor cell samples have been collected and stored for research purposes for decades. Thus, biobanks, which are centers that hold collections and store biological materials representative of the associated diseases, have been established. [4] Research using biobank samples aims to improve the understanding of disease etiology and advance personalized medicine, thus enabling patients to benefit from the rapid therapeutic translation of the research findings. [5] The integrity and quality of biospecimens are ensured through proper sample collection, processing, storage and management. [6] Their quality directly affects the accuracy and reliability of the research findings. [7, 8]

Models are required to evaluate the effectiveness of drugs developed for treating CNSTs. Because testing such drugs directly in patients is challenging, medical professionals use live cells in laboratory conditions as the first preclinical stage to screen potentially effective drugs. [9] These commercially available tumor cell lines have been used for decades to fulfil this purpose. However, studies have shown that long–term culture of live tumor cells results in the formation of independent genetic compositions and microecosystems. In contrast, primary tumor cell lines, which are live cells that are directly retrieved from patients and grown for a limited time in vitro, exhibit the most conserved genomic similarities to the patient's disease. [10]

Several international biobanks with CNSTs primary tumor cell lines were established. [11, 12] Because differences in genetic composition can influence drug treatment outcomes and CNSTs cell lines related to the Middle Eastern genetic pool are rare, we set out to establish our local CNSTs biobank. [13, 14]

Our study aimed to collect samples from patients with CNSTs attending our institution to establish a local biobank for translational research pertinent to patients with CNSTs. Additionally, we intend to facilitate national and regional collaborations to enhance translational research and targeted medicine for patients with CNSTs.

Materials and Methods

Ethical approval

A total of 111 fresh specimens were collected between February 2013 and December 2021 from patients who received treatment at King Abdulaziz University Hospital (KAUH) in Jeddah. The study project reference no. 976–12 was approved by the Ethical Board of KAUH. The National Committee of Biological and Medical Ethics registration number was HA–02–J–008. A signed informed consent form, designed according to the Declaration of Helsinki, was obtained from each patient for each tumor sample donation.

Collection procedure

The sample collection workflow was standardized (Figure 1). All instruments required for the laminar flow hood were set up before collection. When the neurosurgeons reached the tumor site via stereotactic biopsy or craniotomy, they transferred the fresh tumor specimen to a designated labelled container and immersed it immediately on ice in a biohazard ice box. Each specimen was delivered to the laboratory within 10 min by a research team member, while ensuring that it was maintained at 4°C. Another sample was extracted and sent to the hospital laboratory for pathological examination. Representative hematoxylin and eosin (H&E)–stained images of histological variants were obtained by specialized neuropathologists, and specimens were diagnosed according to the WHO classification (Supplementary figure 1).

For processing the Fresh tissue, each tumor specimen was placed in a 100 mm Petri dish under sterile conditions. The weights, sizes, and features of the specimens were recorded. Specimen images were taken at 1× magnification using an Olympus Stereo SZX10 microscope and an Olympus U–TV0 camera. Each sample was divided into three equal pieces (XYZ), and each piece was further cut into three parts (xxx, yyy, and zzz) for analysis. One piece was then taken from each region and grouped as (xyz). One group was used for Ribonucleic Acid (RNA) analysis, the second was stored for in situ tissue and Deoxyribonucleic acid (DNA) analysis, and the third was processed to initiate live cell culturing. This allowed the generation of relatively representative distributed samples that corresponded across the three routes of analysis.

Procedure for tissue preparation for RNA analysis

For RNA analysis (Figure 1B), the tissue samples were cut into smaller pieces (if possible, sized approximately no

more than 0.3 cm) and immersed in RNAlater solution (Life Technologies) and stored at room temperature overnight. A volume of 1 tissue/5–10 volumes of RNAlater was used, and the samples were transferred to genomic facilities for further processing and analysis. Gene expression data for several samples were deposited at the National Center for Biotechnology Information Gene Expression Omnibus under the accession numbers (GSE77259, GSE100534, and GPL6244), and related analyses were published. [15, 16, 20–22]

Procedure for tissue preparation for DNA and immunostaining analysis

For in situ tissue analysis (Figure 1C), the grouped specimens were transferred into cryovials, clearly labelled, and stored at –80°C. For analysis, an in situ immunofluorescence protocol was followed, and data for several tissues were published. [15, 17, 19] DNA was analyzed in several tissues, and exome sequencing data were deposited in the Sequence Read Archive initiated by the National Center for Biotechnology Information under the accession number PRJNA630560. [18]

Procedure for in–vitro primary tumor cell culture initiation

A general protocol for initiating all primary cell lines was established (Figure 1D). Using a blade and tweezers, each piece of blood clot or vessel, gross necrosis, bone, burned tissue, and other visibly contaminated materials were removed from the sample. Each sample was washed with 2 ml of 1x Hank's Balanced Salt Solution (HBSS) (calcium– and magnesium–free; Invitrogen). This step was repeated when the tissue was highly vascular or hemorrhagic in nature. The buffer was removed, and each specimen was minced as much as possible using a sharp, surgical blade. Cut tissues were immersed in 2.5 ml of 1x dissociation cocktail per ~0.5 mm^3 tumor (Dissociation cocktail x10:0.2 mg/mL DNase type 1 (2000 U/mg), Sigma; 0.4 mg/mL collagenase type 1a (125 U/mg), Gibco; HBSS 10 mL (calcium and magnesium–free), Invitrogen). All tissues, including any residues, were collected and transferred to a 50–ml falcon tube, which was incubated in a 37°C incubator while rotating upright for 20 min. The timing of this step was affected by humidity and the general laboratory temperature. The tube was observed and checked for tissue dissociation into cells until the cocktail turned cloudy and the tissue lumps disappeared. The cell mix was then transferred into a 15–ml Falcon tube and centrifuged at 1000 rpm for 3 min at room temperature. The centrifuged liquid was removed and carefully disposed of, ensuring that the pellet was not dislodged. The pellet was resuspended in 5 ml of Dulbecco's Modified Eagle Medium/Nutrient Mixture F–12 (DMEM–F12) (Gibco), 10% FBS (HyClone), 100 U/ml penicillin, and 100 µg/ml streptomycin, and transferred to a T12.5 flask. Other media combinations have been tested; however, no significant effects on cells were observed with alternative combinations. [19] Any filtration prior to this point reduces the chance of culture survival, especially for low–grade tumors. The cell culture flasks were incubated at 37°C in a 5% CO2 incubator overnight. The next day, the culture was observed, and colonies or lumps of tissue were frequently observed. Occasionally, blood cells were observed to float in the media at this stage. All media, including the floating cells, were removed and replaced with fresh DMEM–F12. The medium was then changed every 72 hours at a ratio of 50:50 old to new media. Any clumps disappeared, and all cells separated and moved away from each other within a week after initiation. Once the cells reached subconfluence, they were passaged at a 1:2 ratio. Cell numbers were tracked during this process. When cell growth increased, the dilution ratio also increased. The degree of confluency, morphology, and absence of microbial contamination were monitored continuously. Images were captured at 10× magnification using a Leica DMI6000 microscope and a Leica DFC425 camera.

Documents used to establish and maintain the biobank

Several documents were used to assess and record the samples included in the bank. The recorded information included the clinical characteristics of the patients and their samples, pathological descriptions, weekly cell culture follow–up reports, and an overall report of primary tumor cell lines. In addition, a live tumor cell report form was used to communicate the sample information to the associated clinicians (Supplementary Figure 2). Individual reports were generated to link the different methods applied to each sample (Figure 1E).

Statistical analysis

Data were analyzed using SPSS version 26.0 (IBM Corporation, Armonk, NY, USA). Descriptive statistics, including means, standard deviations, ranges, and percentages, were presented. Complications were categorized, quantified, and presented as frequencies and percentages. To compare the differences between the samples in relation to their histopathological classifications, a t–test was used to assess significant differences in the characteristics of the specimens. The chi–square test was used to evaluate the disparities between variables. Statistical significance was set at $p < 0.05$.

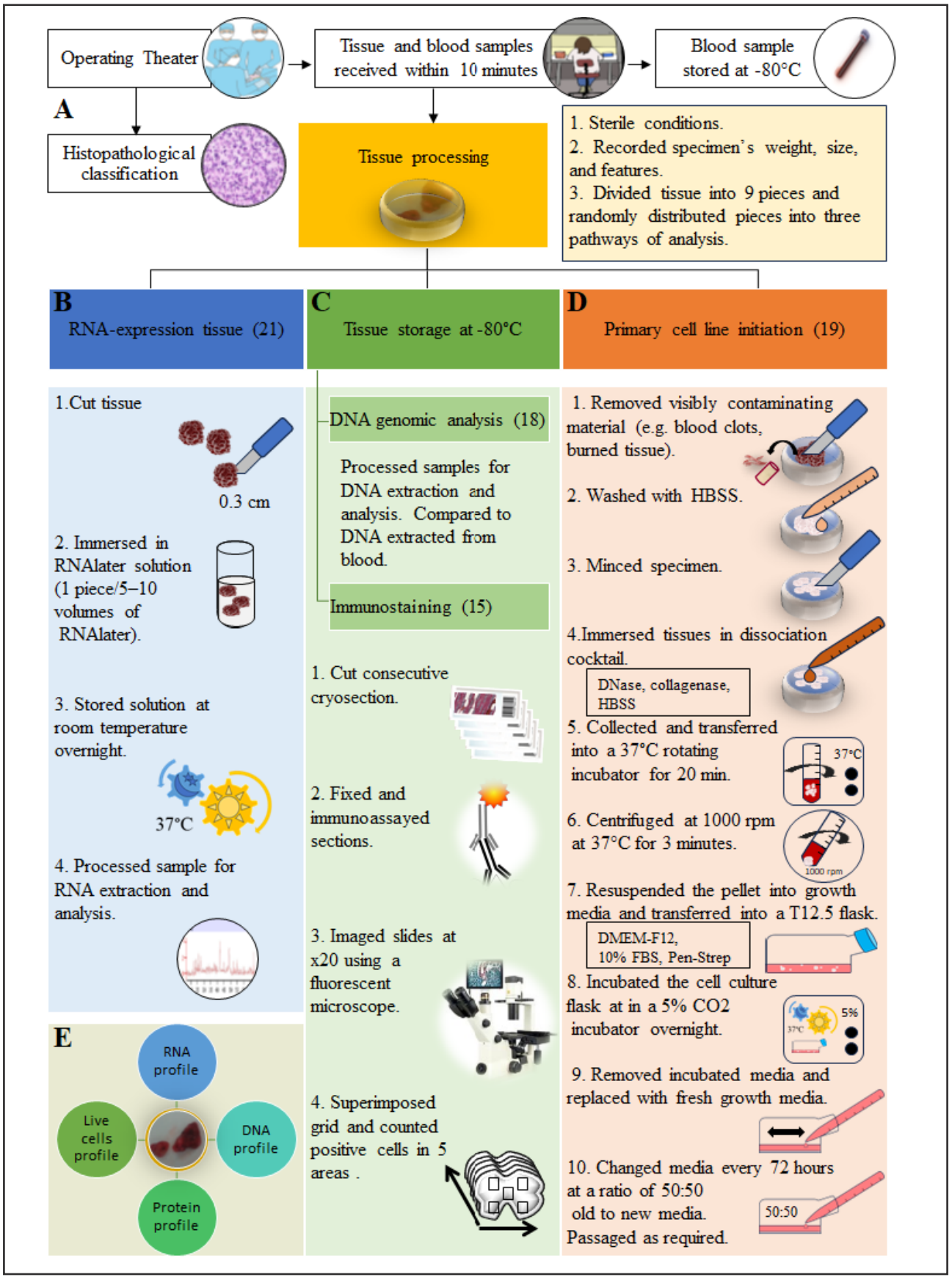
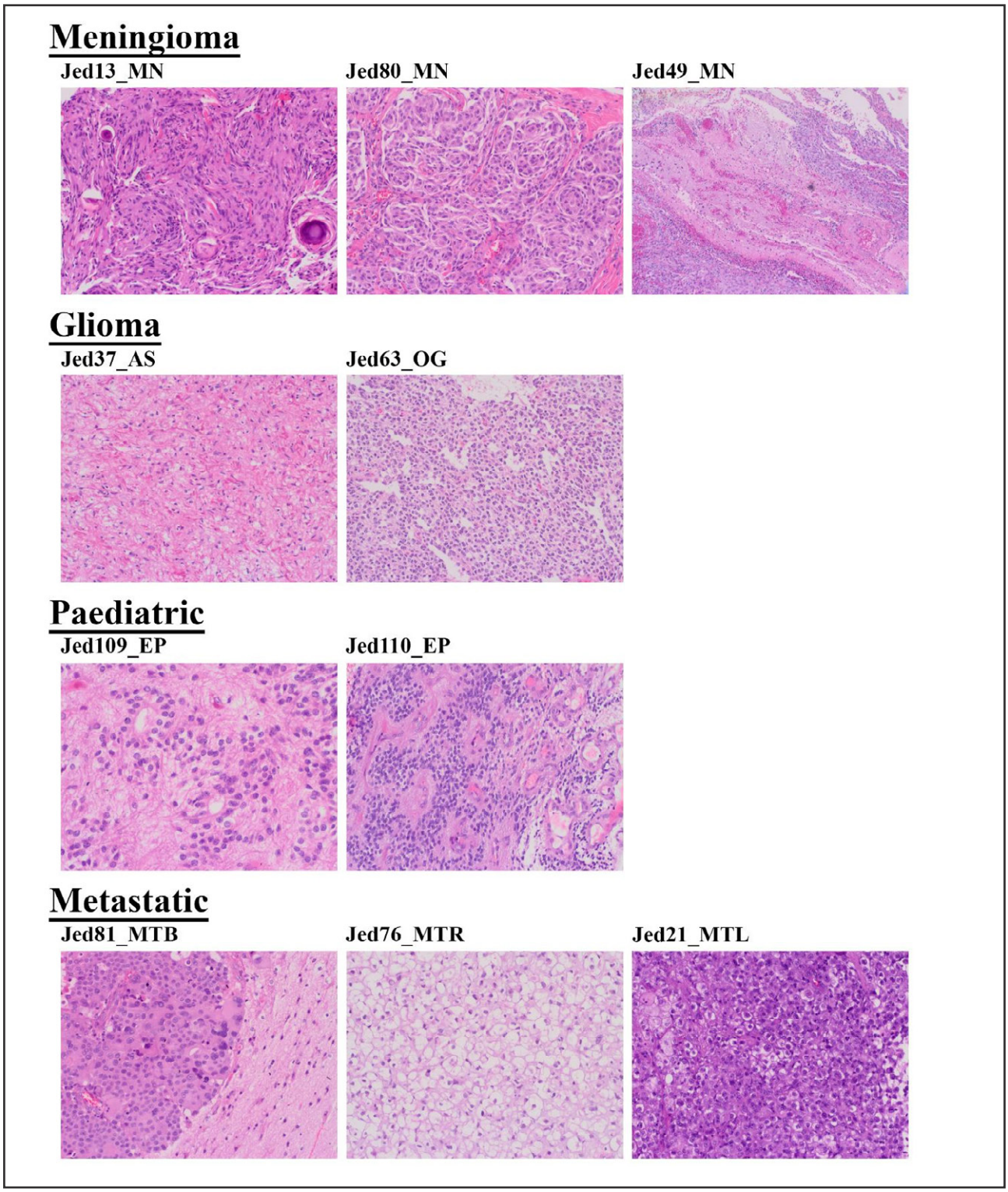


Figure 1. A portrait showing the applied protocols used to initiate a four–dimensional multipurpose CNST biobank. A) Collection and stem tissue preparation procedure. B) Tissue preparation for RNA analysis. C) Tissue preparation for DNA and in situ tissue analyses. D) General protocol used to initiate all primary cell lines. E) Different profiles that can be investigated by following the outlined procedures on a single–tissue sample.

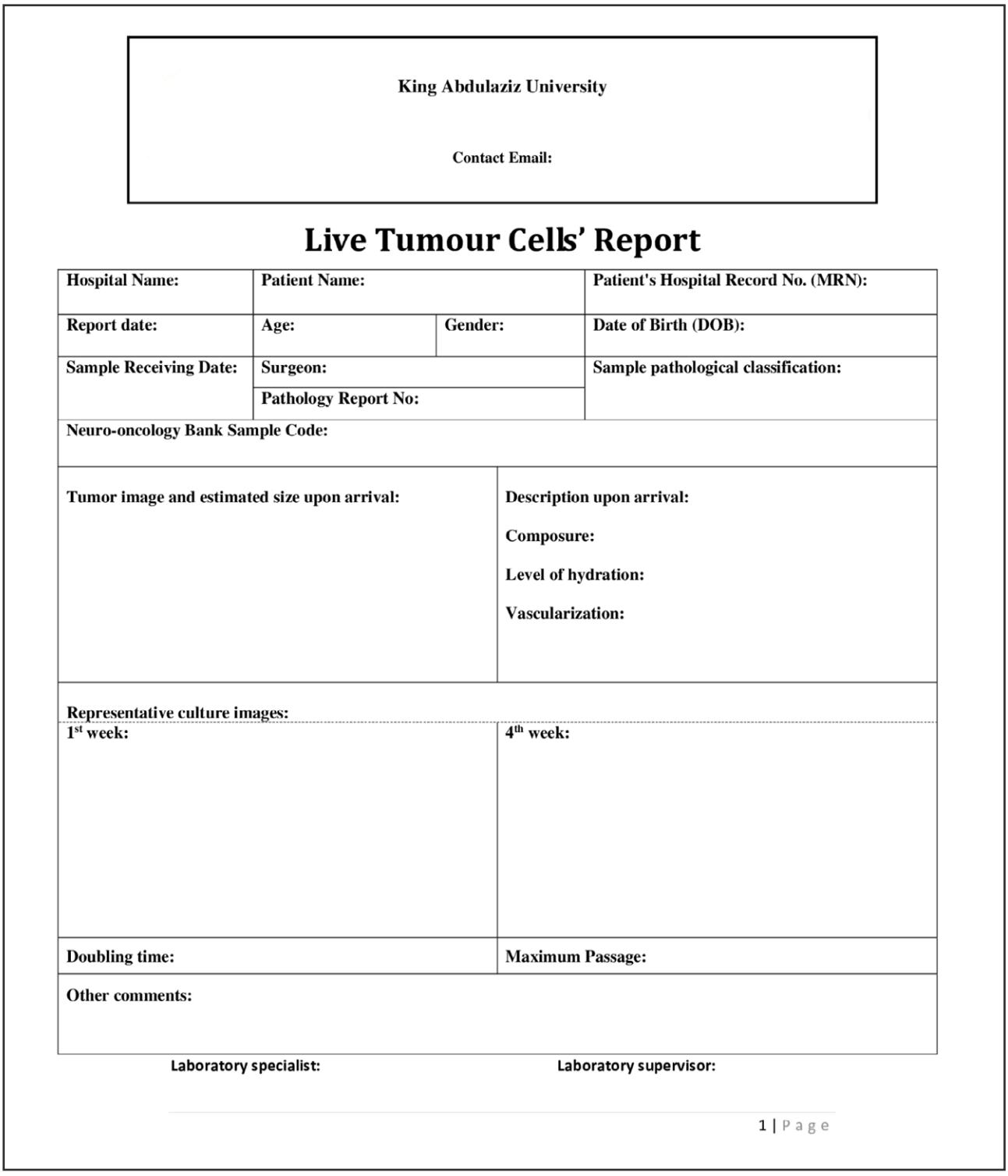


Supplementary Figure 1. Histopathological images of several tissue samples were obtained.

Results

Characteristics of the samples collected in the biobank

The biobank samples had a wide range of characteristics. The clinical characteristics are presented in Figure 2. The sex ratio was 61:39% (female to male). The age range was similarly distributed from birth to 60 years, whereas the number of samples for patients above 60 years was markedly lower. Most samples were from tumors of primary location in the CNS (88 samples); however, there were also samples for recurrent tumors (15 samples) and tumors of non–CNS origin that metastasized to the brain (eight samples). The most frequently collected histopathologically classified



King Abdulaziz University

Contact Email:

Live Tumour Cells' Report

Hospital Name:	**Patient Name:**		**Patient's Hospital Record No. (MRN):**
Report date:	**Age:**	**Gender:**	**Date of Birth (DOB):**
Sample Receiving Date:	**Surgeon:**		**Sample pathological classification:**
	Pathology Report No:		
Neuro-oncology Bank Sample Code:			
Tumor image and estimated size upon arrival:	**Description upon arrival:** **Composure:** **Level of hydration:** **Vascularization:**		
Representative culture images:			
1st week:	**4th week:**		
Doubling time:	**Maximum Passage:**		
Other comments:			

Laboratory specialist: **Laboratory supervisor:**

1 | Page

Supplementary Figure 2. A live tumor cell report form was used in this biobank.

group was meningioma (47 samples), followed by gliomas (12 samples of glioblastoma, 10 samples of oligodendroglioma, and 8 samples of astrocytoma). For meningiomas, a range of histopathological subtypes were collected, with meningothelial tumors being the most frequent (n = 11). The origins of metastatic brain tumors varied, with most samples originating from breast cancer (four samples).

The basic characteristics of the tumor tissue samples were not defined by their origin. Tumor volume, composition, hydration, and vascularization were observed for each tumor sample upon arrival (Figures 3 and 4). The average volumes of the most frequently collected tumors were not significantly different (meningioma, 5.6±1.5 cm^3; glioma, 4.3±1.2 cm^3; pediatric, 3.8±1.3 cm^3; metastatic, 3.9±1.2 cm^3). When observing composition, which represents the

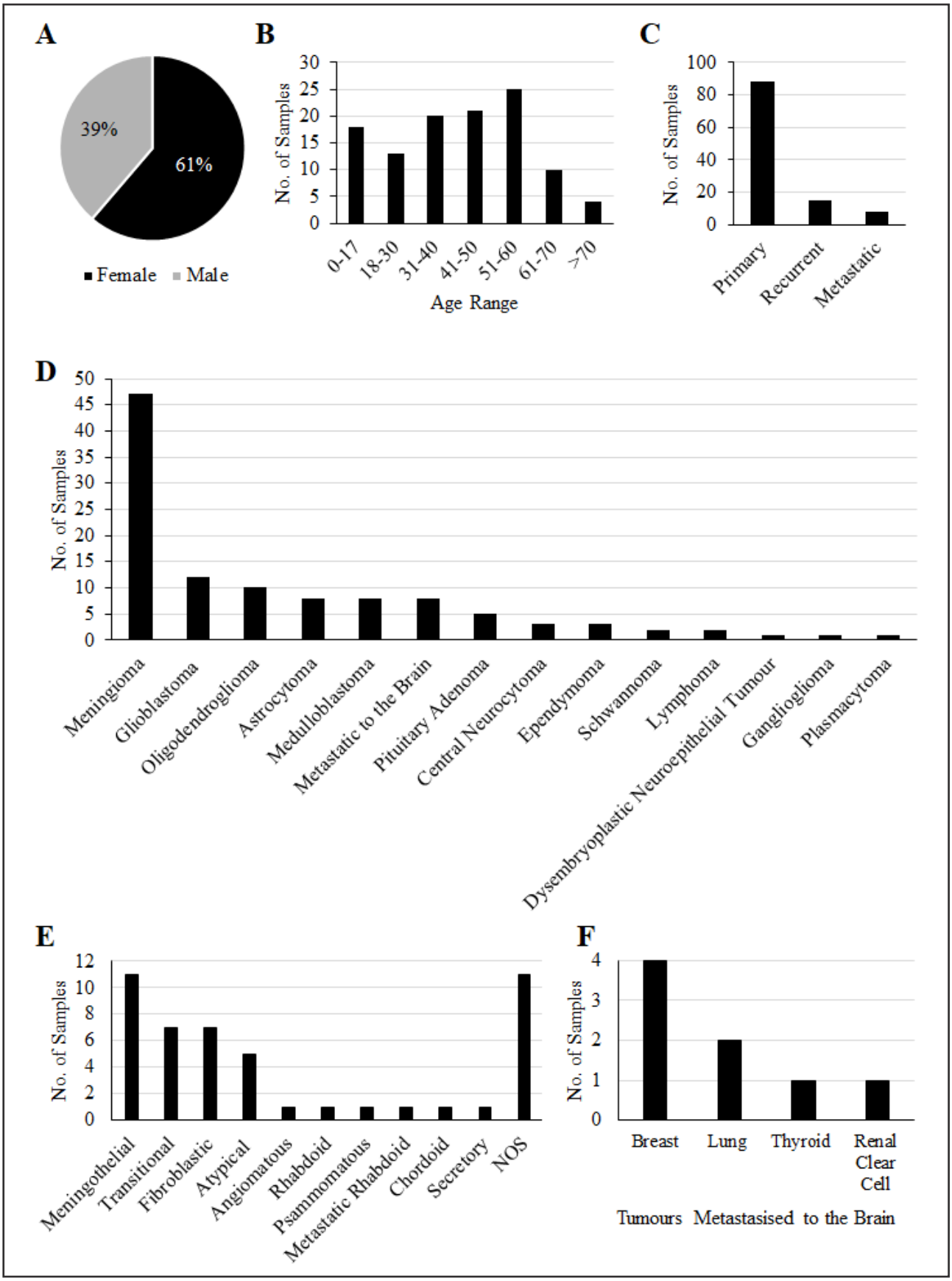


Figure 2. Clinical characteristics of the collected samples. A) Pie chart showing the distribution by sex. B) Bar graph showing the number of samples in the age range of the patients. C) Bar graph showing the number of samples for each tumor according to their frequency of occurrence. D) Bar graph showing the total sample number for each CNST WHO–classified type. E) Bar graph showing the number of samples for each meningioma WHO–classified subtype. F) Number of samples for each metastatic tumor according to the origin.

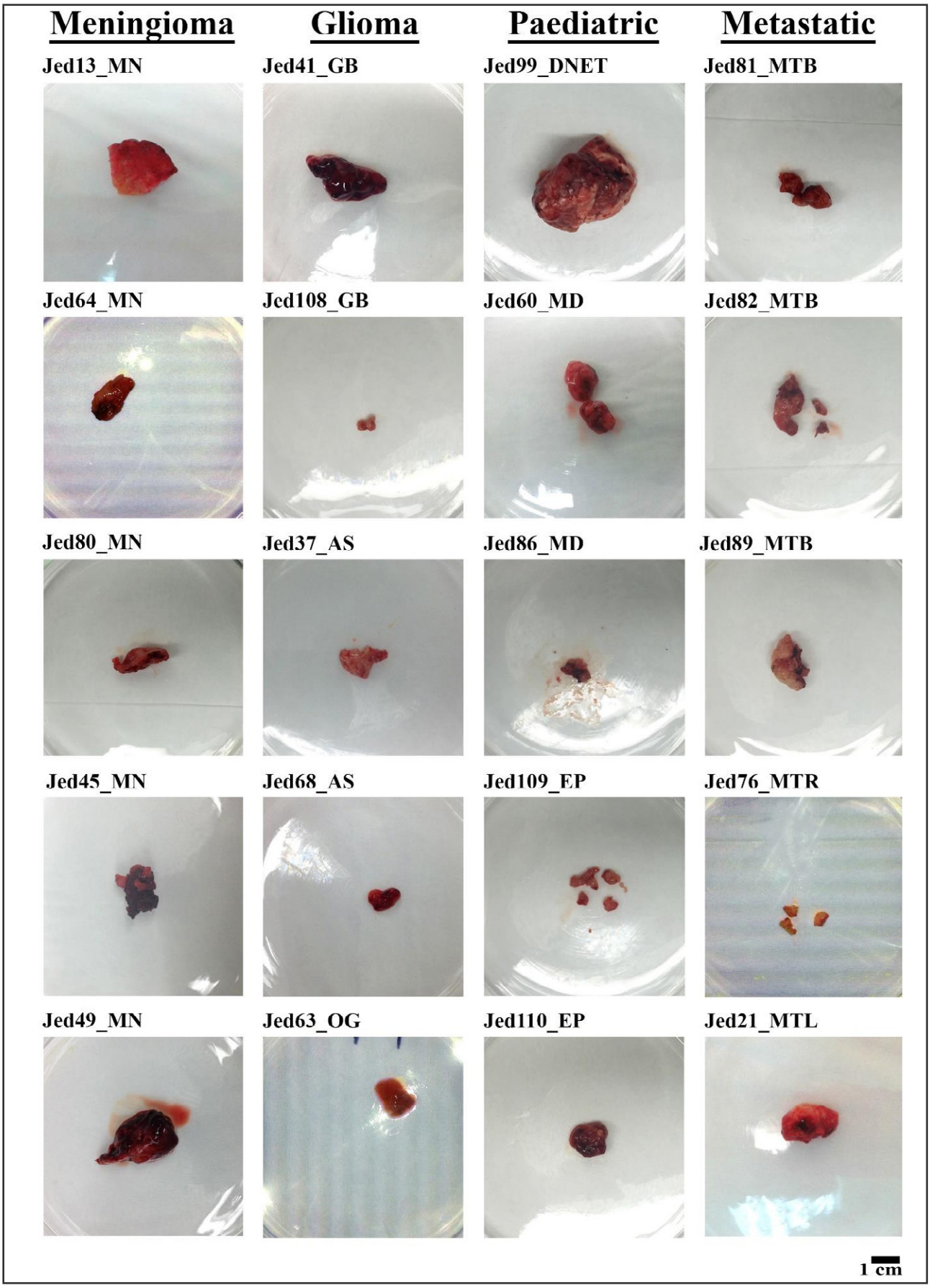


Figure 3. Examples of tissue specimens included in the biobank are as follows: images of tumor samples were taken upon arrival at the biobank laboratory. Selected images were randomly chosen to represent each major CNST group. Images were taken at 1× magnification.

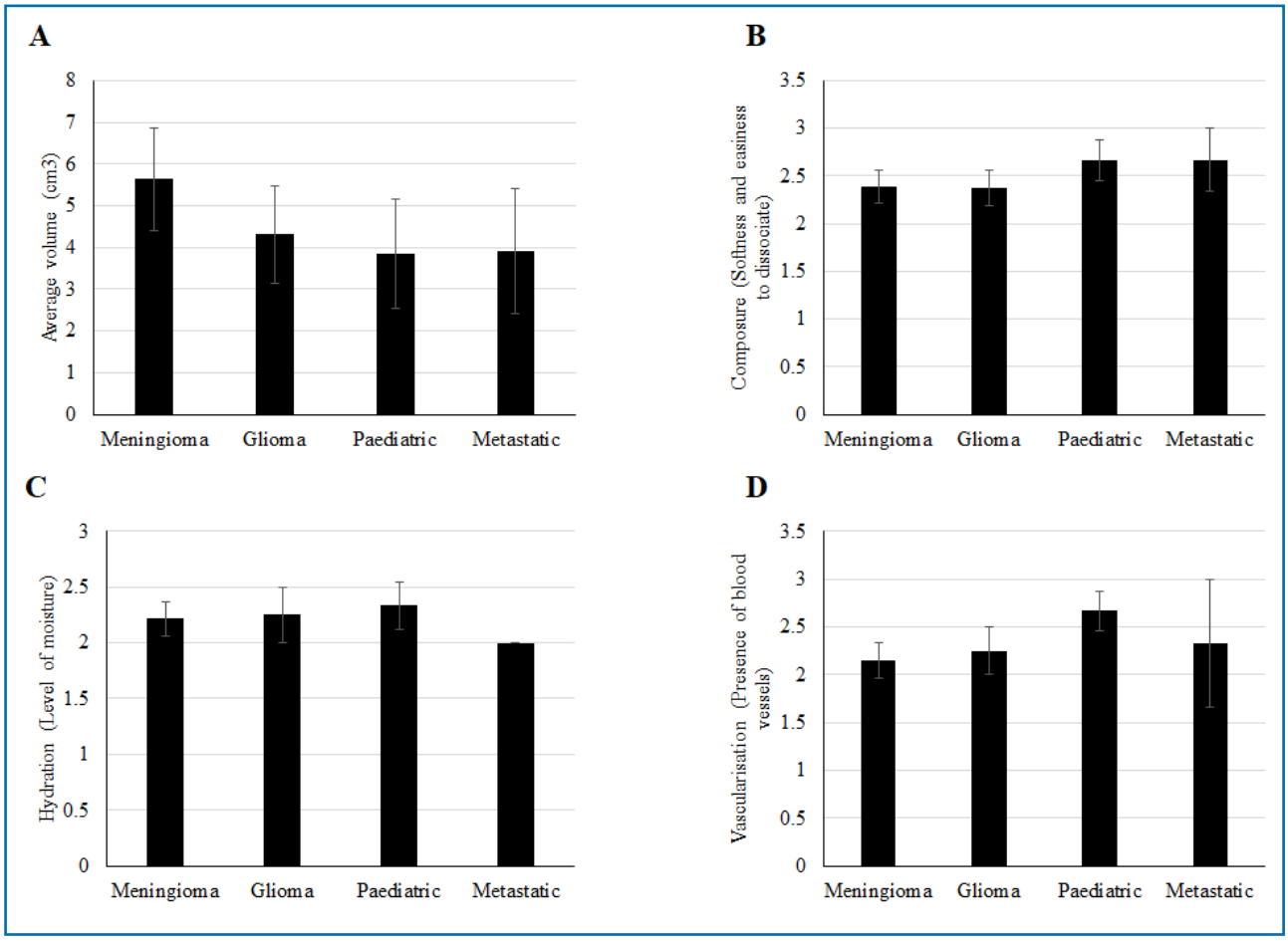


Figure 4. Tissue assessment was performed upon arrival at the laboratory. A) Bar graph showing the average volume measured upon arrival for tumors within each major CNST group. B) Bar graph showing the composition, representing the degree of softness and ease of tissue dissociation. A value of 1 represents hard, bone–like tissue, and a value of 3 represents highly soft and easy–to–dissociate tissue. C) Bar graph showing hydration as assessed by the moisture levels in the samples. A value of 1 represented dry tissue, and a value of 3 represented wet tissue. D) Bar graph showing the degree of vascularization, reflecting the presence of blood vessels in the samples. A score of 1 represented a lack of blood vessels, whereas a score of 3 represented the detection of many blood vessels.

degree of softness and ease of dissociation, tumors that belonged to the most frequently collected groups scored similarly (meningioma 2.4±0.2, glioma 2.4±0.2, pediatric 2.7±0.2, metastatic 2.7±0.3). When observing the level of hydration as assessed by the level of moisture of the samples, there was no detectable difference for tumors that belonged to the most frequently collected groups (meningioma 2.2±0.2, glioma 2.3±0.3, pediatric 2.3±0.2, metastatic 2±0.01). Similar to the previous parameters, the level of vascularization, which reflects the presence of blood vessels in the samples, was not significantly different for tumors that belonged to the outlined groups (meningioma 2.2±0.2, glioma 2.3±0.3, pediatric 2.7±0.2, metastatic 2.3±0.7).

Primary cell lines for histopathologically different types of tumors can be initiated. Using our standard method for initiating primary cells, histopathologically different tumor types were successfully used to initiate primary tumor cell lines (Figure 5). Five types of cells with morphologically observable characteristics were identified in had morphologically cell lines. Morphologically, the cells were either round and mitotic–like, bipolar and spindle neuronal–like, small and flat oligodendrocyte–like with short spikes or processes, large and cytoplasmic glial–like with few processes, or small and cytoplasmic astrocytic–like with long processes. Additional morphologies were observed in primary cell lines derived from brain metastatic tumors. Many primary cell lines have been analyzed and reported. [16–19]

Discussion

Our study established the first four–dimensional multipurpose CNSTs biobank in Saudi Arabia. We collected samples from patients with CNST attending KAUH and

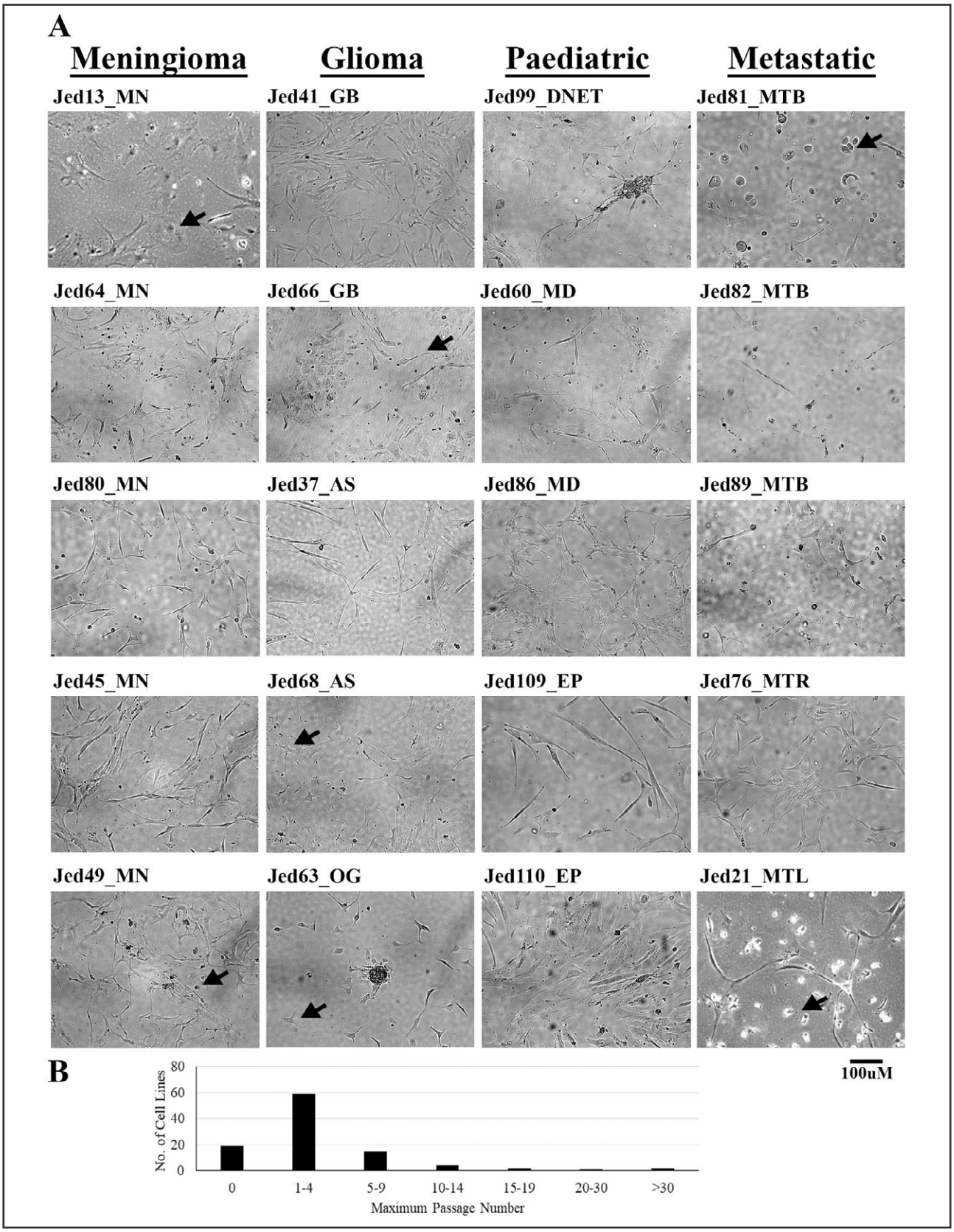


Figure 5. Examples of retrieved cultures. (A) Phase–contrast images of cells after the initiation period. Images were taken at 10× magnification. The arrows indicate differences in morphologies. Jed13_MN: A cell with a large cytoplasm with glial–like cell with a large cytoplasm and few or no processes; Jed49_MN: A round mitotic–like; Jed66_GB: A bipolar spindle neuronal–like cell; Jed68_AS: A long process with small cytoplasmic regions and astrocytic–like cell; Jed63_OG: A small flat with short spikes or processes oligodendrocyte–like cell; "Jed81_MTB: A" group of mammary–like cells; Jed21_MTL: A squamous–like cell. B) Barograph showing the passage range of the cell lines stored in the biobank.

created a local biobank in Jeddah that can be used for national translational research relevant to patients with CNSTs in the future. The protocol–related documents used for reporting and maintaining the samples are presented. A sample collection procedure was used to establish primary tumor cell lines from various types of CNSTs The clinical and sample characteristics of the biobank are demonstrated. Tumor tissue sample parameters and morphologies of primary cell lines were analyzed and are presented.

The establishment of a biobank necessitates adherence to ethical principles. [23, 24] This includes compliance with guidelines for informed consent, privacy protection, and regulatory frameworks. [8] Standardization and harmonization of biobanking procedures are crucial for the comparability and reproducibility of research findings and for fostering global collaboration and data sharing. [25, 26] We considered these procedures when establishing an in vitro cell CNSTs biobank. Thus, the study was approved by the Ethical Board of KAUH prior to any collection, and a signed informed consent form was obtained prior to the sample processing. Confidentiality was respected, and all professionals who handled the collected samples signed a confidentiality agreement. In addition, we created documents to communicate the cell culture findings to the associated clinicians.

In the Gulf and Middle East Arab regions, the establishment of biobanks is limited and is frequently associated with individuals affiliated with universities, hospitals, or non–profit organizations. However, these biobanks lag behind those in developed countries in terms of their pace and quality. [27] The establishment of a biobank incurs significant costs, necessitating initial funding for infrastructure development and sustained funding to ensure long–term viability. Training personnel is crucial for maintaining quality and is often obtained from institutions in Europe or the USA. [25] In Jordan, the King Hussein Cancer Center established the first ISO–compliant cancer biobank in the Middle East through international collaboration, leading to advancements in this field. Efforts are being made to establish biobanks in the Gulf region, such as King Fahd Medical City in Riyadh, which focuses on storing tissues from common solid tumors for future research. [28]

To the best of our knowledge, no biobanks in Saudi Arabia utilize in vitro primary tumor cell lines derived from CNSTs. When comparing the characteristics of the samples between our biobank and the regional banks, several observations were noted. For example, although males are more likely to be diagnosed with CNSTs than females, both regionally and globally, our bank has collected a greater proportion of adult females with 70% predominance. [29] In contrast, our biobank has more male pediatric tumor samples than female samples. The average age of the patients in our biobank was 6.5 and 47 years for pediatrics and adults, respectively, which is comparable to the reported mean age in Saudi Arabia, with 7.4 and 45.64 years for children and adults at the time of diagnosis, respectively. [30] In Saudi Arabia, meningiomas (28.44%) and glioblastomas (25.36%) are the most common primary adult tumors. Our results showed corresponding data, where the most frequently diagnosed CNSTs in adults were meningiomas (50.5%), followed by glioblastomas (10.7%). In Saudi Arabia, low–grade gliomas, followed by medulloblastomas, are the most frequent CNSTs in children and adolescents (27.34% and 26.62%, respectively). This trend is similar to the characteristics of our biobank samples, with low–grade gliomas (astrocytoma, gangliogliomas, oligodendrogliomas, and dysembryoplastic neuroepithelial tumors) accounting for 44.4% of the samples, followed by medulloblastomas (33.3%). Medulloblastomas were the most common single entity in our pediatric samples, consistent with previous reports. [3, 30]

In our preliminary published results, we did not find any significant differences in tumor tissue size, blood vascularization, or hydration. These characteristics did not reflect the type or grade of the tumors. In contrast, each extracted tissue sample appeared unique. In contrast, cell lines derived from the same histological group shared similarities in terms of cell shape and size, as assessed using a previously published guide for primary cell morphology. [19] They also represented the aggressiveness of the tumors by how fast they grew; the higher the tumor grade, the faster the primary growth rate. We also noticed morphological variations between the retrieved tumor cell lines in culture; for example, mammary cells were observed in primary cell lines of tumors retrieved from metastases from breast to brain. This is consistent with the notion that primary tumor cell lines maintain the genetic composition and gene expression of original tumor cells. Concordantly, we previously showed that when testing whether a cell line was representative of its original tumor, the cell line had an 89.2% similarity between its single nucleotide variants (SNVs) and the corresponding tissue. In contrast, the dysembryoplastic neuroepithelial tumor cell line had only a 32.4% average similarity with SNVs in exomes retrieved from 14 meningioma tissues. Thus, the comparative analysis of SNVs indicated that the DNA collected from the primary tumor cell line is highly representative of the corresponding tissue–derived DNA. [16] In our recent publication on the prediction of meningioma recurrence, we encountered two interesting findings. [31] We reported the initial potential association

or proposed causal link between previous scalp traditional cautery and the development of meningioma in two patients after two decades, which requires further verification. [32] We compared the differential gene expression values between two affected and 22 control meningioma cases. In total, 323 genes were statistically differentially expressed in the affected cases compared to the other meningiomas. Of the differentially expressed genes, 231 were downregulated and 92 were upregulated. Of all the differentially expressed genes, DNAJC15 (DNAJ heat shock protein family (Hsp40) member C15) was the most significantly downregulated gene, and MGC32805 (uncharacterized LOC153163), HOMER1 (homer scaffold protein 1), and VEPH1 (ventricular zone expressed PH domain containing 1) were the most significantly upregulated genes in two patients who developed meningiomas with a history of traditional scalp cautery in childhood. [32] Another case was reported of a WHO grade 1 meningioma that transformed to grade 3 with vertebral metastasis. In the tumor stem cell immunofluorescence examination, we observed the expression of Ki67, nestin, CD133, Sox2, vimentin, and Frizzled–9 in tissues collected from the second and third recurrences, which could be a factor in this rapid transformation. [33]

Establishing a CNSTs biobank with primary tumor cell lines presents many challenges, such as the need for significant resources, including funding and skilled personnel. Cultural taboos and unfamiliarity with medical research processes in developing countries hinder patient participation in clinical trials. Public awareness is crucial for understanding ethical considerations, consent regulations, and patient privacy. The time–consuming isolation and storage of primary cells require careful handling to maintain their viability. Cell–economical methods limit extensive cell usage, and the limited availability of clinical data makes thorough analysis challenging. Managing primary CNSTs in an in vitro biobank requires careful planning, substantial resources, and consideration of various limitations. [24]

Limitations

The strength of our retrospective analysis of a prospectively tumor cells collection lies in the establishment of the first biobank for CNSTs in Saudi Arabia. However, our study had some limitations. The relatively small sample size reflects collection being limited to working hours. Many cases performed as emergency surgeries or during off–working hours and weekends were not included. Logistic barriers between institutions are another factor affecting the increase in sample collection. The project was significantly affected by the COVID–19 pandemic. In addition, uninterrupted funding remained an important factor in maintaining this project. Additionally, molecular profiling of patients with CNSTs is being increasingly utilized as a diagnostic tool, supported by different pathology projects that should be combined with our project.

Conclusion

Establishing an in vitro biobank is a frontier in understanding the biology of CNSTs, collecting a range of histologically variable tumor cells. The biobank is a valuable resource for translational research, and we have published data on the DNA, RNA, and morphological features of tumor cell lines and their corresponding tissues for several samples. The biobank will expand collaborations to improve translational research and targeted medicine for national and regional CNSTs patients and encourage other regional centers to reproduce similar biobanks and understand the behavior of CNSTs in the Arab region.

Abbreviations:

CNST: central nervous system tumors; CSCs: cancer stem cells; KAUH: King Abdulaziz University Hospital; SPSS: Statistical Package for the Social Sciences; WHO: World Health Organization; HBSS: Hank's Balanced Salt Solution; DMEM/F–12: Dulbecco's Modified Eagle Medium/Nutrient Mixture F–12; SNVs: single nucleotide variants; RNA: Ribonucleic Acid; DNA: Deoxyribonucleic Acid.

Acknowledgements:

We would like to thank the KFMRC administration and technical departments for their support, particularly M–Zaki Mustafa El Assouli.

Author Contributions:

Conceptualization: DH, SB, MB, FA, MS, AJ, GD, AC, and AA. Data curation and methodology: DH, RA, IK, MA, HQ, and NM. Formal analysis: DH, AA and MA. Funding acquisition: DH, SB, MB, FA, MS, and TA. Supervision: DH, TZ. Validation: DH. Writing (original draft): DH, AA, and MA. Writing (review and editing): DH, IK, AJ, SB, MB, FA, MS, TZ, GD, AC, and AA. All authors have read and approved the manuscript.

Ethics approval:

This study was approved by the Ethics Board of King Abdulaziz University Hospital (board registration no. at the National Committee of Bio– and Medical Ethics: HA–02–J–008; Project reference no. 976–12).

Consent for publication:Not applicable.

A signed informed consent form, designed according to the Declaration of Helsinki, was obtained from the primary relatives.

Availability of data and materials:

The datasets used and/or analyzed in the current study are available on the NIH database, as mentioned in the Methods section.

Competing interests:

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

Funding:

This project was supported by the Strategic Technologies Program of the National Science, Technology, and Innovation Plan in Saudi Arabia (grant number 13–MED2427–03) and the Science and Technology Unit at King Abdulaziz University for the technical support provided to the authors.

References

1. Global Cancer Observatory: Cancer Today. [Internet] cited 2024 Jan 3. Available from: https://gco.iarc.fr/today.
2. Ostrom QT, Price M, Neff C, Cioffi G, Waite KA, Kruchko C, Barnholtz–Sloan JS. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2015–2019. Neuro–oncology. 2022;24(Suppl 5):v1–v95.
3. Saudi Health Council, National Health Information Center, Saudi Cancer Registry. Cancer Incidence Report Saudi Arabia 2020. Riyadh; 2020
4. Caixeiro NJ, Byun HL, Descallar J, Levesque JV, de Souza P, Soon Lee C. Health professionals' opinions on supporting a cancer biobank: identification of barriers to combat biobanking pitfalls. Eur J Hum Genet. 2016;24(5):626–32.
5. Laugesen K, Mengel–From J, Christensen K, Olsen J, Hougaard DM, Boding L, et al. A Review of Major Danish Biobanks: Advantages and Possibilities of Health Research in Denmark. Clin Epidemiol. 2023;15:213–39.
6. Mohamadkhani A, Poustchi H. Repository of Human Blood Derivative Biospecimens in Biobank: Technical Implications. Middle East J Dig Dis. 2015;7(2):61–8.
7. Rush A, Spring K, Byrne JA. A critical analysis of cancer biobank practices in relation to biospecimen quality. Biophys Rev. 2015;7(4):369–78.
8. Mendy M, Lawlor RT, van Kappel AL, Riegman PHJ, Betsou F, Cohen OD, Henderson MK. Biospecimens and Biobanking in Global Health. Clin Lab Med. 2018;38(1):183–207.
9. Goetz LH, Schork NJ. Personalized medicine: motivation, challenges, and progress. Fertil Steril. 2018;109(6):952–63.
10. Kim SC, Cho YE, Shin YK, Yu HJ, Chowdhury T, Kim S, et al. Patient–derived glioblastoma cell lines with conserved genome profiles of the original tissue. Sci Data. 2023;10(1):448.
11. Jacob F, Salinas RD, Zhang DY, Nguyen PTT, Schnoll JG, Wong SZH, et al. A Patient–Derived Glioblastoma Organoid Model and Biobank Recapitulates Inter– and Intra–tumoral Heterogeneity. Cell. 2020;180(1):188–204.e22.
12. Neal JT, Li X, Zhu J, Giangarra V, Grzeskowiak CL, Ju J, et al. Organoid Modeling of the Tumor Immune Microenvironment. Cell. 2018;175(7):1972–88.e16.
13. Niu N, Wang L. In vitro human cell line models to predict clinical response to anticancer drugs. Pharmacogenomics. 2015;16(3):273–85.
14. Almarri MA, Haber M, Lootah RA, Hallast P, Al Turki S, Martin HC, et al. The genomic history of the Middle East. Cell. 2021;184(18):4612–25.e14.
15. Alamir H, Alomari M, Salwati AAA, Saka M, Bangash M, Baeesa S, et al. In situ characterization of stem cells–like biomarkers in meningiomas. Cancer Cell Int. 2018 May 25;18:77.
16. Hussein D, Alhowity A, Algehani R, Salwati AAA, Dallol A, Schulten HJ, et al. A paediatric dysembryoplastic neuroepithelial tumour (DNET) with deregulated stem cell markers: a case report. Transl Pediatr. 2022;11(6):1040–9.
17. Hussein D, Alsereihi R, Salwati AAA, Algehani R, Alhowity A, Al–Hejin AM, et al. The anterior gradient homologue 2 (AGR2) co–localises with the glucose–regulated protein 78 (GRP78) in cancer stem cells, and is critical for the survival and drug resistance of recurrent glioblastoma: in situ and in vitro analyses. Cancer Cell Int. 2022 Dec 8;22(1):387.
18. Hussein D, Dallol A, Quintas R, Schulten HJ, Alomari M, Baeesa S, et al. Overlapping variants in the blood, tissues and cell lines for patients with intracranial meningiomas are predominant in stem cell–related genes. Heliyon. 2020;6(11):e05632.
19. Khan I, Baeesa S, Bangash M, Schulten HJ, Alghamdi F, Qashqari H, et al. Pleomorphism and drug resistant cancer stem cells are characteristic of aggressive primary meningioma cell lines. Cancer Cell Int. 2017 Jul 21;17:72.
20. Schulten HJ, Bangash M, Karim S, Dallol A, Hussein D, Merdad A, et al. Comprehensive molecular biomarker identification in breast cancer brain metastases. J Transl Med. 2017;15(1):269.
21. Schulten HJ, Hussein D, Al–Adwani F, Karim S, Al–Maghrabi J, Al–Sharif M, et al. Microarray Expression Data Identify DCC as a Candidate Gene for Early Meningioma Progression. PLoS One. 2016;11(4):e0153681.

22. Schulten HJ, Hussein D, Al–Adwani F, Karim S, Al–Maghrabi J, Al–Sharif M, et al. Microarray expression profiling identifies genes, including cytokines, and biofunctions, as diapedesis, associated with a brain metastasis from a papillary thyroid carcinoma. Am J Cancer Res. 2016;6(10):2140–61.

23. Coppola L, Cianflone A, Grimaldi AM, Incoronato M, Bevilacqua P, Messina F, et al. Biobanking in health care: evolution and future directions. J Transl Med. 2019;17(1):172.

24. Vodosin P, Jorgensen AK, Mendy M, Kozlakidis Z, Caboux E, Zawati MH. A Review of Regulatory Frameworks Governing Biobanking in the Low and Middle Income Member Countries of BCNet. Biopreserv Biobank. 2021;19(5):444–52.

25. Dagher G. Quality matters: International standards for biobanking. Cell Prolif. 2022;55(8):e13282.

26. Annaratone L, De Palma G, Bonizzi G, Sapino A, Botti G, Berrino E, et al. Basic principles of biobanking: from biological samples to precision medicine for patients. Virchows Arch. 2021;479(2):233–46.

27. Abdelhafiz AS, Ahram M, Ibrahim ME, Elgamri A, Gamel E, Labib R, Silverman H. Biobanks in the low– and middle–income countries of the Arab Middle East region: challenges, ethical issues, and governance arrangements–a qualitative study involving biobank managers. BMC Med Ethics. 2022;23(1):83.

28. Sughayer MA, Souan L. Establishing an ISO–Compliant Modern Cancer–Biobank in a Developing Country: A Model for International Cooperation. Adv Exp Med Biol. 2015;864:141–55.

29. Ilic I, Ilic M. International patterns and trends in the brain cancer incidence and mortality: An observational study based on the global burden of disease. Heliyon. 2023;9(7):e18222.

30. Almutrafi A, Bashawry Y, AlShakweer W, Al–Harbi M, Altwairgi A, Al–Dandan S. The Epidemiology of Primary Central Nervous System Tumors at the National Neurologic Institute in Saudi Arabia: A Ten–Year Single–Institution Study. J Cancer Epidemiol. 2020:1429615.

31. Alkhotani A, Saeedi R, Alomar H, Alghamdi F, Almaghrabi J, Binmahfoodh M, Baeesa S. Predictors of Recurrence and Long–Term Outcomes of Intracranial Meningiomas: A Retrospective Multicenter Study from Saudi Arabia. Gulf J Oncolog. 2025 Sep;1(49):40–52.

32. Alqurashi A, Baeesa S, Kurdi M, Hussein D, Schulten HJ Intracranial Meningiomas Developed after Traditional Scalp Thermal Cautery Treatment in Childhood: Clinical Reports and Gene Expression Analysis. Gulf J Oncolog. 2022 Jan;1(38):90–106.

33. Baeesa SS, Hussein D, Altalhy A, Bakhaidar MG, Alghamdi FA, Bangash M, Abuzenadah A. Malignant Transformation and Spine Metastasis of an Intracranial Grade I Meningioma: In Situ Immunofluorescence Analysis of Cancer Stem Cells Case Report and Literature Review. World Neurosurg. 2018 Dec;120:274–289.