Concept Paper

Occupational Geroscience: A New Scientific Discipline at the Intersection of Geroscience and Occupational Medicine

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Occupational Geroscience: A New Scientific Discipline at the Intersection of Geroscience and Occupational Medicine

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Abstract

Occupational Geroscience is proposed here as a new scientific discipline at the intersection of geroscience and occupational medicine. It studies how chronic occupational exposomes activate the hallmarks of aging in workforces with defined biological hazards. The primary outcome is the slope of multi-clock estimators of biological age over a career-length follow-up in an exposed cohort versus a matched unexposed comparator. Hallmark-specific markers (γ-H2AX, telomere length, SASP cytokines, cf-mtDNA) are measured alongside, and each worker's lifetime dose record is linked to the biomarker series. Existing exposome aging studies measure population scale environmental drivers without isolating defined occupational cohorts. Existing occupational radiation cohorts measure cancer mortality without measuring biological aging. What is missing is a longitudinal outcome that spans systems, is anchored in the hallmarks of aging, and is tied to a defined occupational exposome with prospective dose data; such an outcome has not yet been established. That gap motivates naming the field. The founding case is fluoroscopy guided interventional medicine. Scatter ionising radiation, biomechanical loads, psychological strain, and material co-exposures plausibly activate several hallmarks of aging across careers that involve thousands of procedures. Cell and animal studies support key elements of the mechanism. Working populations have not yet been studied prospectively, and a cohort study is needed to test the prediction directly. This paper defines Occupational Geroscience by its object, methods, and predictions, and sets inclusion and exclusion criteria. The research agenda begins with a population-level registry and a modular longitudinal biomarker cohort. Shielding analyses can then be nested within the cohort, while tiered radiosensitivity profiling and biological mitigation trials, including the antioxidant pre-exposure trial (Study 5), should follow only after feasibility, safety, and primary cohort signals are established. The interventional studies are hypotheses to be tested, not proven preventive methods.

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1. The Unnamed Problem

Does the work itself age the worker? The question emerges from four decades in immunology and clinical research, medical devices, and radiation safety, as well as direct personal experience of radiation induced occupational injury. A prior argument for comprehensive head, eye, and neck protection in fluoroscopy-guided procedures (Yu, 2020) made the clinical case for anatomically complete shielding without addressing the broader biological aging burden considered here.

Colleagues have been forced into early retirement with illnesses that may have been connected to their work. Others have died of cancers arising in the organs most exposed to scatter radiation across careers of thousands of fluoroscopically guided procedures. These remain unproven causal claims, but they have not been ruled out either, because medicine has lacked the conceptual tools and the research agenda to ask the question.

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An interventional cardiology fellow stands hours per case in a scatter field under a loaded lead apron. Like aircrew on transpolar routes, she absorbs ionising radiation she cannot perceive; unlike aircrew, she also accumulates biomechanical strain and material co-exposures specific to the cath lab. The pattern is the same: delayed damage, no perceptible warning, regulatory compliance standing in for biological safety. The chronic risk becomes part of professional identity, and workers come to accept it as the price of the profession.

The question is whether the occupational exposome accelerates biological aging itself across whole teams, not only primary operators, and in ways open to measurement and intervention. Existing approaches address cancer endpoints and physical dose limits, and do so incompletely. The biological aging question is not yet addressed at all.

2. Defining Occupational Geroscience

Occupational Geroscience is more than a research programme within geroscience or a sub-specialty of occupational medicine. Four features distinguish it.

Object of study. Whether specific workplace exposomes alter biological aging across the working life. The primary outcome is a cohort-level pattern of change in biological age, interpreted alongside markers of DNA damage, telomere attrition, mitochondrial stress, senescence associated inflammation, and clonal hematopoiesis. For early cohort selection, workforces are prioritised when exposure plausibly engages three or more López-Otín hallmarks. The threshold is a pragmatic screening rule rather than a biological law.

Methods. Longitudinal cohort designs combining biological age clocks, hallmark-specific assays, and individual exposure records from career entry through repeated visits. A core biomarker stack pairs validated epigenetic clocks with proteomic, inflammatory, metabolomic, and glycomic aging measures, alongside hallmark-specific assays (γ-H2AX, leukocyte telomere length, SenMayo transcriptomic signatures, SASP cytokines, cf-mtDNA, and error-corrected CHIP sequencing). The aim is not to prioritise any single marker but to test whether occupational exposure produces a reproducible multisystem aging signature.

Endpoints. Cohort level biological age pace attributable to a work exposome; dose-response relationship with anatomical laterality where applicable; and within cohort modulation by intervention.

Predictions. The proposal makes four testable predictions. Exposed operators should age biologically faster than matched unexposed physicians, and the signal should scale with cumulative individual dose. Anatomical patterns should track known dose laterality. Expanded shielding should attenuate the effect at the cohort level. The risk should also extend beyond the primary operator to other exposed team members. Any prediction can fail; failure is informative.

Geroscience, occupational medicine, and radiation protection each supply useful tools, but each treats only part of the question. Geroscience does not condition on occupational exposomes. Occupational medicine has not adopted the hallmarks framework as an outcome. Radiation protection focuses on dose limits and cancer endpoints. Section 4 develops the gap analysis.

3. Terminology: Exposome and the Hallmarks of Aging

The exposome. Wild (2005) coined "exposome" as the environmental counterpart to the genome: the totality of non-genetic exposures shaping health from conception onward. The occupational exposome is the work environment subset. For an interventionalist it has several components. The principal agent is scatter ionising radiation. Other chronic exposures include the mechanical load of heavy lead aprons and other personal protective equipment, prolonged standing and awkward posture, procedural psychological strain, and disrupted sleep from on call schedules. Cervical, lumbar, and lower limb disorders are reported at high prevalence in fluoroscopy exposed staff (Klein et al., 2015; Orme et al., 2015; Monaco et al., 2020), and chronic mechanical loading and persistent pain in turn drive inflammation, sleep disruption, and reduced functional reserve, all

 doi:10.20944/preprints202605.0287.v1

relevant to geroscience outcomes. Chemical co-exposures arrive by several routes: lead from aprons (dermal contact and inhalation from aged materials), PFAS from protective garments and surgical drapes, volatile organic compounds from equipment and disinfectants, residual anaesthetic gases from hybrid theatres, and PM2.5 from hospital environments. The hallmarks of aging should be applied to this full exposome, not to radiation alone.

Other workplace exposures should be measured alongside scatter radiation rather than treated as background. In interventional settings the relevant set includes apron load, prolonged standing, static posture, night work, work stress, cleaning and disinfectant agents, and surgical smoke. These exposures can affect musculoskeletal, inflammatory, respiratory, sleep, or functional outcomes that overlap with aging measures. Evidence is uneven. In one cross-sectional study of hospital female nurses, night shift work was not associated with biological age overall, but age acceleration increased with years of night shift work among nurses with overweight/obesity, work stress, or both (Carugno et al., 2021). Exposure to cleaning and disinfectant agents is better established as a cause of work-related asthma, with spray products carrying additional risk (Mwanga et al., 2024). Surgical smoke contains respirable particulate and gaseous hazards, though long-term cancer risk in staff remains uncertain (Limchantra et al., 2019). These exposures should be recorded, adjusted for in cohort analyses, and reduced where practical.

The hallmarks of aging. López-Otín and colleagues proposed nine hallmarks in 2013 and twelve in the 2023 update: genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, disabled macroautophagy, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, altered intercellular communication, chronic inflammation, and dysbiosis. Geroscience holds that these mechanisms converge through common upstream pathways to drive cardiovascular disease, cancer, neurodegeneration, and metabolic syndrome. Aging in this sense refers to the progressive shift toward chronic disease, functional decline, and loss of physiological reserve, rather than to chronological time. An exposome that activates multiple hallmarks simultaneously is therefore both a candidate carcinogen and a candidate aging accelerant, with consequences for every age-related disease.

Radiation in the modern geroscience literature. Beyond its long-recognised role as a carcinogen, ionising radiation is among the most widely used experimental tools for inducing cellular senescence in vitro and modelling aging phenotypes in vivo. Recent reviews conclude that radiation-induced and natural cellular senescence share common molecular features: persistent DNA damage response signalling, mitochondrial dysfunction, SASP secretion, and altered miRNA and epigenetic profiles (Ibragimova et al., 2024; Guan et al., 2025; Li et al., 2018). The mechanism in cell and animal systems is well established. Its operation at chronic occupational dose rates over career length intervals remains untested.

Mitochondria as integrators. Among the twelve hallmarks, mitochondrial dysfunction carries integrative weight. Picard and Shirihai (2022) describe mitochondria as a cellular information-processing system that senses endogenous and environmental inputs, integrates them through network-level interactions, and generates output signals tuning nuclear gene expression and inter-organ physiology. This paper abbreviates that model as MIPS for brevity. The abbreviation is a manuscript shorthand introduced here rather than an established field acronym. Mitochondrial output signals modulate the expression of a substantial fraction of nuclear genes, so damage propagates well beyond the organelle. Scatter radiation generates reactive oxygen species and mitochondrial DNA lesions in parallel with nuclear DSBs, making the MIPS a candidate amplifier of occupational radiation injury.

4. The Missing Intersection

Adjacent literatures address pieces of the question without integrating them. Pandics et al. (2023) reviewed how environmental drivers from air pollution to occupational exposures accelerate biological aging and drive cardiovascular and cerebrovascular pathology. Argentieri et al. (2025) integrated environmental and genetic architectures of aging and mortality at population scale. In the

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UK Biobank, the exposome explained substantially more variation in mortality and proteomic aging than polygenic risk did for several major outcomes. The Semmelweis Study (Ungvari et al., 2024) is the first large scale longitudinal occupational cohort framed within the geroscience hallmarks. Its target population is university employees aged 25 and above, not professions defined by chronic activation of multiple hallmarks. DNA methylation studies in shift workers and firefighters, the NIOSH exposome initiative, and Andrasfay et al. (2023) on occupational characteristics and biological aging contribute related fragments.

Occupational safety for medical radiation workers operates within a separate regulatory framework built on effective dose limits, ALARA principles, and cancer risk estimates derived from the linear no-threshold model (BEIR VII, 2006; ICRP 103, 2007). It monitors cumulative physical dose and reports cancer incidence, but does so imperfectly: the cancer surveillance infrastructure for medical radiation workers is incomplete (Section 6).

The Distinct Contributions

Occupational Geroscience proposes a primary outcome that no current field measures: a multisystem, hallmark anchored, longitudinally measured biomarker series tied to a specific occupational exposome with prospective dose linkage. That is the central gap. Existing exposome aging studies (Argentieri 2025; Pandics 2023; Andrasfay 2023) typically associate aggregate environmental exposures with one or two biological age measures at a single time point. Existing occupational radiation cohorts (e.g., INWORKS) focus on cancer and circulatory mortality. Occupational Geroscience treats the cohort level pace of multi-clock biological aging in an exposed workforce as its primary outcome, paired with concurrent hallmark-specific markers.

A second contribution is a measurement standard that no parent field currently specifies. The proposed biomarker panel covers six domains: epigenetic clocks, cytogenetic and molecular markers, vascular and ocular markers, neurocognitive and psychological function, functional reserve, and individual cumulative dose mapping. The panel is measured at career entry and at five-year intervals under uniform protocols. Panel validation is among the early tasks (Section 8).

The justification for naming a new field is the combination of these elements: prospective dose linkage at the individual level, multi-clock longitudinal measurement of biological aging, career-length follow-up tied to a defined occupational exposome, and falsifiable predictions about anatomical laterality and intervention response. No single element on its own has been enough to motivate a separate discipline, but together they describe an object of study that none of the parent fields currently addresses.

A third contribution is prediction. Dose laterality offers the cleanest test: left-cranial dose excess in invasive cardiologists should produce a left-cranial signal in biomarkers and outcomes. That claim cannot be derived from general population exposome aging studies. A second prediction is team level. Nurses and technicians, not only primary operators, should show a measurable biological age signal proportionate to position specific cumulative dose. That distinguishes this proposal from existing radiation protection rules focused on individual dose limits. The shielding attenuation prediction (Study 4) and antioxidant mitigation prediction (Study 5) are the first interventional commitments.

Without prospective data from validated multi-omic biological age panels in radiation exposed medical personnel, the question of whether interventional staff age biologically faster than unexposed controls remains unanswered. Until it is answered, the occupational burden remains unmeasurable to regulators, clinicians, and prospective trainees, and informed professional choice has no evidence base to draw on.

The proposed field can be summarised as a chain from occupational exposure, to candidate mechanisms, to measurable worker outcomes, with measurement domains attached at each step (Figure 1).

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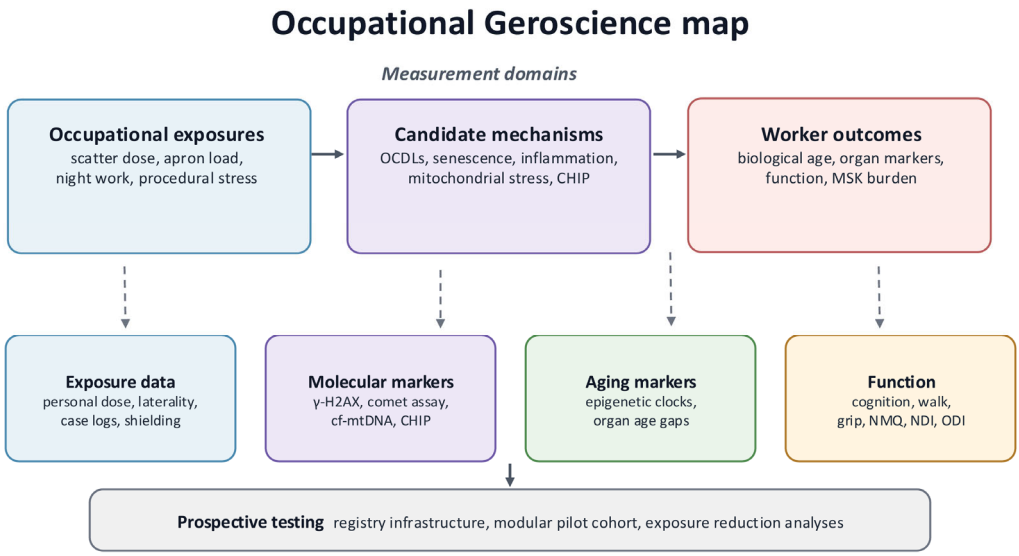


Figure 1. Occupational Geroscience as a conceptual map. The schematic links occupational exposures in interventional medicine to candidate biological mechanisms, worker outcomes, and proposed measurement domains. Arrows indicate proposed links for prospective testing rather than proven one-way causality.

5. Why Interventional Medicine Is the Founding Case

A new field needs a founding case: a specific occupational group, a specific exposome, and a mechanism understood well enough to support the first empirical programme. Interventional medicine satisfies all these conditions.

The team present during each fluoroscopically guided procedure includes the primary operator, nurses, radiographers, and scrub technicians. Complex cases may also involve an anaesthesiologist, an industry representative, and a second operator. The primary operator, standing closest to the radiation source, receives the highest individual dose. Nurses and technicians at fixed positions beside the table accumulate clinically meaningful lifetime exposures, though typically at lower per-procedure doses. Andreassi and colleagues (2016) documented significantly elevated rates of skin lesions, cataracts, orthopaedic illness, and anxiety and depression across the cath lab workforce, with risk rising with duration of exposure. Successive SCAI membership surveys reported at least one orthopaedic injury in roughly half of practising interventional cardiologists. Cervical spine, lumbar spine, and hip, knee, and ankle injuries each clustered at career-relevant rates and increased with age and case volume (Goldstein et al., 2004; Klein et al., 2015). A multisite case-control study at Mayo Clinic found musculoskeletal pain related to work in 54.7% of interventional staff versus 44.7% of unexposed clinical employees (adjusted OR 1.67, 95% CI 1.32 to 2.11). The highest burden was among technicians (62%) and nurses (60%), exceeding rates in attending physicians (44%) and trainees (19%) (Orme et al., 2015). A scoping review of protective apron use across radiology, cardiology, electrophysiology, and endoscopy reported elevated rates of spinal symptoms and musculoskeletal discomfort among apron-wearing staff, with no complete consensus on direct causation (Monaco et al., 2020). Causal attribution to the apron alone is hard to establish from any single study. These surveys are cross-sectional and largely conference recruited and are therefore subject to selection and recall bias; the prospective registry proposed in Section 8 is designed to address those limitations. On the available data, the burden extends across the team rather than being confined to the primary operator, and both radiation and apron mechanisms appear to contribute.

This combined pattern is the substantive content behind the ALARA+ idea (Salavitabar et al., 2026). Conventional ALARA targets scatter dose. ALARA+ aims at total occupational harm, so that protection strategies are judged jointly against radiation, physical load, and ergonomic burden. A configuration that lowers radiation while increasing spinal load, fatigue, or musculoskeletal injury

 doi:10.20944/preprints202605.0287.v1

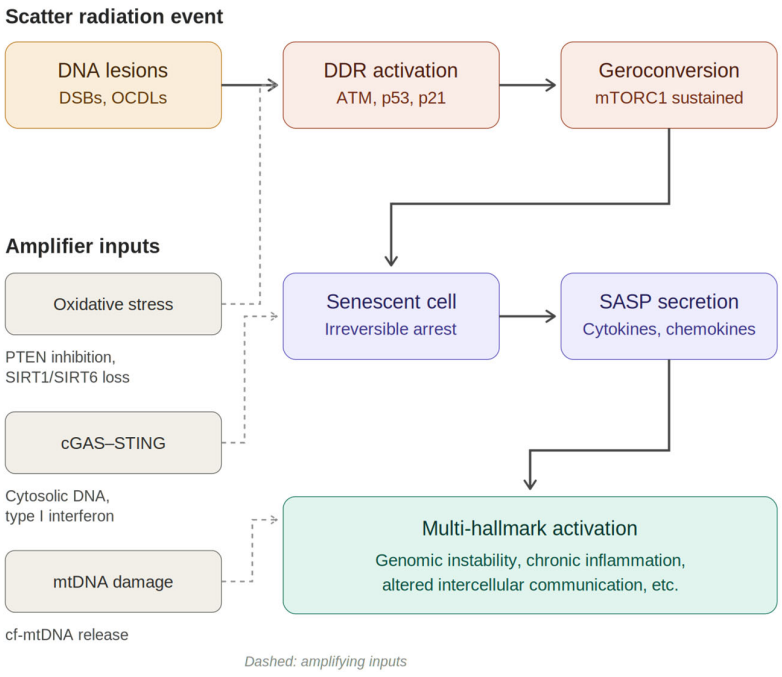
shifts part of the burden rather than removing it. The implication for the present work is to track dose, shielding design, apron load, ergonomics, and long-term worker outcomes together rather than separately.

Mechanism

The biological pathway from acute ionising radiation to senescence is well characterised in experimental systems. Acute exposure at high doses and chronic exposure at low dose rates activate divergent molecular and cellular response programmes (Sampadi et al., 2022), so the relevant question is whether the same cascade operates at the chronic low dose rates over the length of a career typical of occupational scatter exposure; Sections 5–7 address that question.

A scatter event deposits energy in exposed tissue and produces a range of DNA lesions: base damage, single-strand breaks, double-strand breaks (DSBs), and oxidatively generated clustered lesions (OCDLs) where multiple damage sites occur within one or two helical turns. DSBs trigger the apical damage response. OCDLs are more challenging to repair than isolated lesions and can accumulate when ROS exceed repair capacity, contributing to persistent DNA damage response signalling (Sedelnikova et al., 2010; Georgakilas et al., 2013). Persistent damage activates the DNA damage response (DDR) through ATM kinase signalling, engaging the p53–p21 axis to halt the cell cycle while repair is attempted. If mTORC1 signalling remains active during this arrest, the reversible arrest is converted into irreversible senescence regardless of whether repair succeeds; this is the geroconversion pathway (Blagosklonny, 2012). Senescent cells secrete the senescence associated secretory phenotype (SASP), a chronic pro-inflammatory secretome that propagates aging signals and engages multiple López-Otín hallmarks (Figure 2).

Earlier work showed that even at low doses, ionising radiation produces clustered damage in human cells, including oxidized base and abasic site clusters, with cluster class frequencies comparable to frank DSBs (Sutherland et al., 2000). Subsequent reviews of non-DSB clustered damage indicate that these lesions can slow base excision repair, persist longer than isolated lesions, and sometimes be processed into additional DSBs at replication (Eccles et al., 2011). Enzyme-modified comet assays and related oxidative cluster readouts are therefore candidate biomarkers for chronic occupational exposure, though they should be treated as investigational rather than established clinical tests.



 doi:10.20944/preprints202605.0287.v1

Figure 2. The geroconversion–SASP cascade. Persistent DNA damage from scatter radiation activates the DNA damage response (DDR); sustained mTORC1 signalling during damage-induced cell-cycle arrest converts reversible arrest into irreversible senescence (geroconversion). Senescent cells secrete the senescence associated secretory phenotype (SASP), propagating aging signals across tissue and engaging multiple hallmarks of aging. Three classes of amplifier input feed into the cascade at the indicated stages and are characteristic of chronic low dose rate occupational exposure: oxidative stress (PTEN inhibition, SIRT1/SIRT6 loss); cGAS–STING activation by cytosolic DNA and radiation-induced micronuclei; and mitochondrial DNA damage with cf-mtDNA release.

Three classes of amplifier may extend this cascade beyond what acute high-dose models predict, though direct demonstration in working populations is not yet available. Sustained oxidative stress inhibits PTEN and reduces SIRT1 and SIRT6, sustaining mTOR activation across repeated exposures (Barnes, 2019); NF-κB drives SASP transcription, with mTOR contributing through promotion of IL-1α (IL1A) translation (Laberge et al., 2015). Cytosolic DNA fragments and micronuclei induced by radiation activate the cGAS–STING pathway, driving type I interferon signalling and chronic inflammation (Dvorkin et al., 2024; Ibragimova et al., 2024; Guan et al., 2025). The same events that damage nuclear DNA also generate ROS and lesions in mitochondrial DNA, which lacks protective histones and has reduced repair capacity. Damaged mitochondria release cell-free mitochondrial DNA (cf-mtDNA) and undergo network fragmentation, propagating inflammatory and SASP-promoting signals through the mitochondrial information-processing system (Picard and Shirihai, 2022; Trumpff et al., 2019). All three amplifiers are well supported in cell and animal systems. Direct evidence from interventional staff is still missing.

At 300–500 procedures per year over a 30-year career, an operator accumulates roughly 9,000–15,000 procedures, though peak volume rarely sustains across a full career. The cascade above repeats with each procedure. The senescence decision at the single cell level is discrete (a cell either enters senescence or does not), so cumulative exposure should produce a discrete and growing population of senescent cells rather than a graded organ level response. This prediction has not yet been tested in interventional cohorts.

In operators working standard table orientations, scatter dose is preferentially delivered to left sided cranial structures. The BRAIN study confirmed this lateralised exposure pattern (Reeves et al., 2015). Self-collected case series have reported a striking left lateralised pattern in interventional physician brain tumours (Finkelstein, 1998; Roguin et al., 2013), with 22 of 26 known laterality cases left-sided in Roguin's series. The case series design lacked numerator and denominator data, a limitation the original authors emphasised while calling for systematic study. They nonetheless interpreted the 85% laterality as suggestive of a causal relationship with occupational exposure.

Why the Brain: A Mitochondrial Vulnerability

The lateralised dose pattern is not the only brain finding. Cross sectional neurocognitive testing in long-term cath lab staff has identified deficits in delayed recall, visual short-term memory, and semantic lexical access ability relative to unexposed controls (Marazziti et al., 2015). Tumour laterality and neurocognitive deficits together form the strongest anatomically specific clinical signal in the workforce, concentrated in cranial regions historically least covered by routine shielding. Lead aprons cover the torso, thyroid collars the anterior neck, and eye protection addresses the lens; cranial shielding has not been part of standard care.

The head is also uniquely vulnerable on a mitochondrial basis. The brain consumes about 20% of resting metabolic energy while constituting about 2% of body mass, making it among the most mitochondria-dependent tissues in the body alongside the heart and kidneys. Mitochondrial DNA lacks protective histones, has reduced repair capacity, and carries a mutation rate roughly 10- to 100-fold higher than the nuclear genome (Kam and Banati, 2013). Oxidative mtDNA damage including the 4,977 base-pair common deletion has been reported at low radiation doses. Mitochondria also generate secondary ROS over hours to weeks post-exposure, producing a self-perpetuating damage loop (Kawamura et al., 2018). Adding mtDNA common deletion burden, mtDNA copy number, and

 doi:10.20944/preprints202605.0287.v1

cf-mtDNA to the founding research agenda directly tests for excess mitochondrial damage in the exposed workforce.

6. The Surveillance Gap

A prospective, population-level health-outcomes registry that links individual lifetime dose records to multisystem cancer and noncancer endpoints in interventional medical staff does not currently exist.

Self-collected case series such as Roguin et al. (2013) are informative numerator only signals but cannot substitute for denominator-based surveillance. INWORKS provided the strongest existing evidence for dose dependent circulatory disease mortality (Gillies et al., 2017) and radiation associated leukaemia and lymphoma mortality (Leuraud et al., 2015) in radiation workers. The cohort was nuclear industry personnel, however, and the design did not address the exposure profile, anatomical dose distribution, or outcome laterality of interventional medical staff. National cancer registries include occupational codes but do not link individual radiation dose records to health outcomes in this population. Noncancer endpoints (cataracts, subclinical atherosclerosis, orthopaedic injury, psychological morbidity) that cross-sectional studies have associated with cath lab work at substantially elevated effect sizes (Andreassi et al., 2015, 2016) fall outside any existing registry. The missing instrument is a population level prospective registry that combines a defined denominator, individual lifetime dose records, staff role, room position, beam laterality, procedure type, and multi-system cancer and non-cancer endpoints. Section 8 specifies that design.

Globally, fluoroscopy-guided procedures span interventional cardiology, vascular and interventional radiology, vascular surgery, electrophysiology, neurointervention, urology, gastroenterology, orthopaedics, and pain medicine. The exposed workforce is correspondingly large. UNSCEAR estimated approximately 11.4 million workers monitored for human-made radiation sources worldwide in 2010–2014 (uncertainty interval 6.2–21 million); the medical sector is the largest single subsector (UNSCEAR, 2022, Annex D). In the United States, tens of thousands of physicians work across these fluoroscopy intensive specialties, and the nurses, radiographers, and technicians working alongside them multiply that figure several-fold.

7. What Can and Cannot Currently Be Measured

Epigenetic clocks estimate biological age or its pace from patterns of DNA methylation at specific genomic sites. Several are validated against mortality and chronic disease incidence in large population cohorts. GrimAge predicts mortality (Lu et al., 2019), PhenoAge predicts all-cause mortality, cancer risk, healthspan, and physical functioning (Levine et al., 2018), and DunedinPACE measures pace in biological years per calendar year rather than as a static estimate (Belsky et al., 2022). All three show significant associations between acceleration of biological age and subsequent disease.

Within-individual variability across short measurement intervals is documented (Higgins-Chen et al., 2022). Readings can be affected by acute physiological states, illness, major life events, and technical factors including blood processing and sample handling. A single measurement at one time point should not be read as a definitive measure of an individual's biological age, and clocks are not validated for individual clinical diagnostic use in this context.

The appropriate research approach uses clocks as cohort level instruments. Multiple standardised measurements are taken over career length intervals, with sample sizes large enough that individual variability averages out across groups. A target on the order of several hundred high-volume interventional operators against matched unexposed physician controls is plausible. Paired measurements would be taken at career entry and at 5, 10, and 20 years, using multiple clocks under standardised processing. Final sample size should be set by formal power calculations using DunedinPACE within-individual variance and pace-of-aging variances from comparable physician cohorts; this concept paper does not fix a number.

 doi:10.20944/preprints202605.0287.v1

The cohort level approach is consistent with the recently proposed concept of Peakspan (Zhavoronkov et al., 2026), defined as the interval during which an individual maintains at least 90% of peak functional performance in a specific physiological or cognitive domain. Where healthspan focuses on years lived without debilitating disease, Peakspan draws attention to earlier losses of physiological and cognitive reserve. For an exposed workforce, the relevant question is whether the occupational exposome accelerates loss of biological or functional reserve, well before any diagnosable disease appears.

Organ age models add another layer. Plasma proteomic models can estimate organ age gaps across major systems. In Oh et al., 11-organ models were reproducible across five cohorts of 5,676 adults; nearly 20% showed marked acceleration in one organ, and 1.7% showed multiorgan aging (Oh et al., 2023). In Whitehall II, organ specific age gaps measured in 6,235 midlife participants predicted incident age-related disease and multiorgan multimorbidity over roughly 20 years (Kivimäki et al., 2025). These studies do not show that fluoroscopy guided work causes organ-specific aging, but they justify adding organ specific proteomic signatures to the toolkit. Interventional work exposes tissues unevenly and may stress the lens, brain, vasculature, immune system, and musculoskeletal reserve through different mechanisms.

Alternative biomarkers provide independent individual-level measures and should be incorporated alongside epigenetic clocks. These include leukocyte telomere length, γ-H2AX foci burden, plasma SASP cytokine panels, and mitochondrial DNA copy number.

Multi-omic estimation of biological age. Epigenetic clocks are one omics layer among several. Plasma proteomic clocks predict mortality and age-related disease (Lehallier et al., 2019; Argentieri et al., 2025). The inflammatory iAge clock, derived from cytokine and chemokine profiles, captures immunosenescence (Sayed et al., 2021), and metabolomic aging scores from ^{1}H-NMR profiling outperform conventional cardiovascular risk factors for 5- and 10-year mortality prediction (van den Akker et al., 2020; Deelen et al., 2019). IgG N-glycan profiling provides a low-cost readout of biological age (Krištić et al., 2014). At the transcriptomic level, the SenMayo gene set is a validated 125-gene senescence signature and a candidate readout in PBMC RNA-seq of the geroconversion–SASP cascade (Saul et al., 2022). The variability cautions above apply across layers. Convergence across orthogonal omics layers strengthens cohort-level inference and should be the analytic standard.

8. Founding Research Agenda: Five Priority Studies

The five studies are structured by dependency rather than intended as simultaneous work. The registry (Study 1) and the modular pilot cohort (Study 2) are foundational. Shielding and exposure reduction analyses (Study 4) are designed to nest within the cohort once it is enrolling. Tiered radiosensitivity work (Study 3) and the work on informed consent and career communication (Section 10) are downstream and become appropriate only if the primary cohort hypotheses are supported. The antioxidant pre-exposure trial (Study 5) is also nested in the cohort and remains contingent on safety and pharmacokinetic groundwork.

1. Prospective registry of health outcomes at the population level. A systematic, denominator-based incidence registry for all interventional staff (physicians, nurses, radiographers, and technicians), linked to individual lifetime dose records. Large-scale occupational cancer linkage infrastructures exist; the Nordic Occupational Cancer Study followed about 15 million people across five Nordic countries with 45 years of cancer incidence data (Pukkala et al., 2009). NOCCA links cancer to occupational category derived from census data, however, not to individual lifetime dose records, and does not extend to the non-cancer endpoints that define the burden in interventional medicine. The proposed extension links individual lifetime dose records to multi-system endpoints across all four staff categories. The registry should be society led and KOL supported rather than a single-centre undertaking, with funding from professional societies (SCAI, IRPA, ACOEM, or equivalent), public agencies, and occupational health bodies, and with national cancer registry

 doi:10.20944/preprints202605.0287.v1

coordination as the operational template. This baseline is required before any assessment of biological aging can be set against conventional endpoints.

Exposure Ascertainment and Dosimetry Uncertainty

The first methodological problem is exposure ascertainment: individual exposure must be measured accurately enough to test whether occupational exposure affects aging biology. Dosimeter compliance is a recognised problem in interventional medicine. In a survey of 989 fluoroscopically guided interventional medical workers in Korea, 52.7 percent reported wearing a badge for the entire working time, and the National Dose Registry mean annual effective dose (0.95 mSv) rose to 1.79 mSv after compliance adjustment, an 89.4 percent increase, in a population in which most individual doses sit below the limit (Lee et al., 2022). The general implication is that nonwear can lead to underestimation of recorded dose at the individual and registry level. Beyond compliance, recorded readings depend on badge position (inside versus outside the apron, collar versus trunk, badge height relative to the scatter field), operator height and posture, C-arm angle, patient size, table height, shielding configuration, dosimeter type, and exchange interval; double dosimetry and dedicated eye and extremity monitoring may also be relevant in interventional settings (Carinou et al., 2023). Case-level logs should accompany badge records and should capture operator role, procedure type, fluoroscopy time, cine use, air kerma, dose area product, shielding configuration, and apron type. Without this layer, individual lifetime dose remains an estimate rather than a measurement, and dose-response analyses inherit that uncertainty.

2. Multi-domain biological, functional, and neurological assessment (modular). A prospective longitudinal assessment across the measurement domains below, designed as a modular pilot rather than a single fixed panel. Centres can begin with feasible components, for example dosimetry mapping, epigenetic aging pace, and selected molecular biomarkers, and add further domains as resources, sample handling capacity, and external funding allow. The full panel is the long-term target, not a precondition for starting. The intended assessment cadence is career entry and five-year intervals in interventional lab staff versus matched unexposed controls. The protocol counts as a research output of the field and should be standardised across centres in stages.

Individual Cumulative Dose Mapping

Spatial mapping of scatter doses to brain, thyroid, lens, and gonads across operator, nurse, radiographer, and anaesthesiologist positions, with procedure type, table height, and gantry angulation recorded. Existing dosimetry literature focuses predominantly on primary operators; dose profiles of nurses and technicians at fixed positions across years of procedures are incompletely measured.

Epigenetic Aging Pace

DunedinPACE, GrimAge, and PhenoAge from standardised blood draws at multiple time points with uniform processing protocols. Cohort-level comparisons over years long intervals are the appropriate research unit given documented individual level variability across short intervals.

Cytogenetic and Molecular Biomarkers

γ-H2AX foci quantification, leukocyte telomere length, plasma SASP cytokine panels (IL-6, IL-8, IL-1α, TNF-α), mitochondrial DNA copy number in PBMCs, and circulating cf-mtDNA in plasma or serum. These directly index DNA damage, cellular senescence, chronic inflammation, and mitochondrial stress signalling. cf-mtDNA is a particularly attractive candidate. It is inducible within minutes by acute psychological or physical stress (Trumpff et al., 2019). Its response to chronic occupational radiation exposure has not been characterised.

 doi:10.20944/preprints202605.0287.v1

Vascular and Ocular Markers

Carotid intima media thickness with laterality analysis, slit-lamp grading for posterior subcapsular lens opacities, blood pressure, and fasting lipid panels.

Neurocognitive and Psychological Function

Standardised assessment of delayed recall, visual short-term memory, and semantic lexical access ability, domains in which exposed cath lab staff have shown lower scores in cross-sectional work (Marazziti et al., 2015). Validated instruments for anxiety and depression complete the battery.

Functional Reserve

Grip strength timed up-and-go, and six-minute walk distance as noninvasive measures of physiological reserve.

Musculoskeletal Symptom Surveillance

Musculoskeletal burden related to apron use should be tracked as a secondary outcome alongside radiation dose and the geroscience biomarkers, using questionnaires and clinical assessment rather than imaging. The Nordic Musculoskeletal Questionnaire is administered at career entry and at each five-year visit. The Neck Disability Index and the Oswestry Disability Index are added for workers reporting cervical or lumbar pain during the previous 12 months. A short workload log records apron type and weight, single-piece versus two-piece configuration, fit, hours worn per shift, days per year with pain, analgesic use, and physiotherapy use. Workers with persistent, functionally limiting, or progressing symptoms should be referred to occupational health and physiotherapy under standard pathways. Spine MRI or plain radiography is not indicated in asymptomatic staff and should only be ordered when there is a clinical reason. The aim is consistent symptom surveillance at the cohort level that supports the shielding study (Study 4) and the informed-consent work in Section 10, without turning routine career exposure into a medical investigation.

Multi-Agent Exposome Co-Measurement

Quantitative co-measurement should include blood lead concentration, urinary PFAS panels, urinary metabolites of volatile organic compounds, and personal PM2.5 dosimetry, with collection synchronised to scatter radiation dosimetry intervals. Without measurement, multi-agent exposure remains rhetorical, joint effect modelling cannot be pursued, and any biological age signal cannot be attributed to scatter radiation versus the broader work environment.

Clonal Hematopoiesis of Indeterminate Potential (CHIP)

Error-corrected targeted sequencing of peripheral blood for somatic mutations in haematopoietic stem cells. CHIP is age-associated and predicts all-cause mortality, cardiovascular disease, and haematologic malignancy independently of conventional risk factors (Jaiswal et al., 2014; Genovese et al., 2014). Exposure shapes the mutational landscape: cytotoxic chemotherapy preferentially selects PPM1D-mutant clones (Hsu et al., 2018), and cancer therapy including ionising radiation selects for TP53, PPM1D, and CHEK2 mutations (Bolton et al., 2020), in contrast to the DNMT3A/TET2/ASXL1 spectrum dominant in unselected aging populations (Jaiswal et al., 2014; Genovese et al., 2014). Whether chronic occupational scatter radiation produces a similar selection signature in interventional staff is a directly answerable question. A positive finding would be a molecular fingerprint of cumulative occupational exposure stronger than any single clock of biological age, and would directly link the founding case to the DNA-damage mechanism in Section 5.

 doi:10.20944/preprints202605.0287.v1

3. Tiered individual radiosensitivity assessment (research-grade). The two-panel structure is a research instrument. It is not a deployable occupational screening tool. Both panels require validation in occupational cohorts before any operational use, including evaluation of analytic and clinical validity at occupational dose rates. Baseline functional screening via γ-H2AX foci formation per unit dose provides phenotypic assessment of intrinsic DNA damage response capacity. Genotypic screening complements this in two tiers.

Panel A — Baseline Occupational Radiosensitivity Panel. A common-variant SNP panel, to be validated in an occupational cohort before any operational deployment. If validated, Panel A would yield a polygenic radiosensitivity score across the functional axes of radiogenomics: DNA damage sensing and repair, cell cycle checkpoint control, oxidative stress response, inflammation and SASP tone, vascular response, telomere reserve, and mitochondrial function. Output would be probabilistic and research-grade. The literature behind Panel A (Andreassen and Alsner, 2009; Rosenstein et al., 2014; Kerns et al., 2015; Seibold et al., 2020) was developed in radiotherapy patient cohorts at therapeutic doses. No score from that work has yet shown proven clinical validity even in those settings. Whether such scores carry predictive validity at chronic occupational low-dose-rate exposures is an early empirical task. Final panel composition should require consensus by the Radiogenomics Consortium or equivalent body.

Panel B — Enhanced Occupational Radiosensitivity Panel (clinical-genetics referral pathway). Full-gene sequencing of high-penetrance loci including ATM, BRCA1, BRCA2, the Lynch syndrome genes (MLH1, MSH2, MSH6, PMS2), TP53, CHEK2, PALB2, NBN, and other clinically actionable loci. Panel B is offered to staff meeting any of six criteria: a first-degree relative with cancer before age 50; two or more first- or second-degree relatives with the same cancer; a known familial cancer syndrome; a family history of early-onset cardiovascular disease (men before 55 years, women before 65 years) or neurodegenerative disease; personal history of childhood cancer, radiation-treated malignancy, or unusual tissue reactions; or a Panel A result in the highest tertile. Results are diagnostic-grade, require pre- and post-test genetic counselling, and are released to the worker rather than the institution. Final gene list composition should be developed through formal consensus by the clinical genetics and radiogenomics communities.

Ethical framework. Both panels are structured as worker-controlled health information, consistent with the US Genetic Information Non-discrimination Act and equivalent international protections (EU GDPR Article 9; UK Equality Act 2010 and Data Protection Act 2018; Canadian Genetic Non-Discrimination Act 2017). Institutional research access is limited to aggregate de-identified data. Panel B requires mandatory pre- and post-test genetic counselling. High-penetrance findings warrant individualised shielding intensity, surveillance schedules, and procedural volume considerations; they never warrant career exclusion. The ethical standard is to adjust the intensity of protection rather than to gate access to the career: genetic information, where used, should adjust the intensity of protection and surveillance, never the worker's access to the career.

Precedent. Murphy and colleagues argued in 2017 that interventional neuroradiologists should be screened for germline mutations in DNA repair genes (including BRCA1, BRCA2, MLH1, MSH2, and TP53) before entering radiation-intensive careers (Murphy et al., 2017). Their reasoning was that inherited impairment of repair mechanisms increases the risk of cancer induction from occupational exposure. The proposal was reiterated in 2019 with expanded scope (Murphy and Murphy, 2019). The Murphy proposals provide an early precedent; they should not be read as a deployable occupational screening model. Subsequent radiogenomics work has established that radiosensitivity is polygenic and influenced by variants across at least seven functional categories (Andreassen and Alsner, 2009; Rosenstein et al., 2014; Kerns et al., 2015; Seibold et al., 2020). Functional phenotypic assays such as the standardised G2 chromosomal assay (Pantelias and Terzoudi, 2011; Guogytė et al., 2017) complement genotypic screening. Tissue-specific susceptibility loci, notably the lens crystallins (CRYAA, CRYAB, GJA8) for cataract risk, add an eighth dimension relevant to documented occupational endpoints. ICRP Task Group 111 has now formally placed individual radiosensitivity on the regulatory agenda (ICRP, 2025–2026 Public Consultation Document, draft). The ALARA+

 doi:10.20944/preprints202605.0287.v1

Summit proceedings (Salavitabar et al., 2026) document the multi-system occupational risk profile that this work is designed to address. This body of work supports the larger, prospective, ethically governed validation studies at occupational dose rates proposed here. It does not yet justify them.

4. Shielding configuration and exposure reduction analysis nested in the cohort. A prospective comparison nested within the Study 1 registry and Study 2 modular cohort. The contrast of interest is between higher and lower individual scatter dose and apron load achieved under contemporary practice, rather than a fixed pairing of named devices. Shielding hardware will continue to evolve; the durable comparison is between staff in the lower and upper strata of cumulative individual dose and physical load, however that is achieved at the time of measurement. Primary biological endpoint is pace measured by biological age clocks; primary physical endpoints are individual cumulative scatter dose and an apron load index. Minimum five-year follow-up.

Phantom and clinical dosimetry studies show that several shielding configurations can reduce scatter at defined measurement sites under specified geometries, with reductions varying by device design, staff position relative to the source, beam angle, procedure type, anatomical site, and dosimetry protocol. Single-centre or phantom reductions require independent multi-centre replication before being generalised, and none have been linked to biological aging endpoints in exposed staff. Framing the analysis as a contrast in achieved individual dose and load, rather than as a comparison of specific products, keeps the question testable as the technology base changes.

A second pre-specified rationale concerns musculoskeletal load. Configurations that take some or all of the apron weight off the operator include suspended suits, fixed barriers, and similar gravity-offloading supports. These setups should reduce the cumulative mechanical load on the cervical and lumbar spine seen in this workforce (Klein et al., 2015; Orme et al., 2015; Monaco et al., 2020). Pre-specified secondary endpoints include cervical and lumbar pain, the validated disability indices noted in Study 2, and any change in apron wearing time per shift, alongside the primary endpoint for biological aging. Musculoskeletal outcomes should be analysed separately from the dose-attenuation analysis so that the two mechanisms are not conflated.

A detailed study design is beyond this concept paper. Governance principles for this analysis and Study 5 are stated together in the Conflicts of Interest section: independent steering committee, pre-registered protocol, blinded endpoint adjudication, public data availability, and no involvement of any shielding or antioxidant manufacturer in design, conduct, analysis, or reporting.

5. Antioxidant pre-exposure trial. Physical dose reduction remains the primary prevention strategy. The field should also test whether transient biological mitigation of oxidative injury induced by radiation can attenuate early damage biomarkers.

Oral antioxidant formulations given before diagnostic radiation exposure have reduced γ-H2AX foci in PBMCs (Kuefner et al., 2012; Velauthapillai et al., 2017). NAC reduced γ-H2AX foci in human lymphocytes after low-dose x-ray exposure in vitro and in vivo (Brand et al., 2015). Intravenous NAC given around invasive cardiovascular procedures was associated with suppression of procedure related micronucleus increases despite a higher dose-area product in the treated group (Andreassi et al., 2012). These studies support antioxidant pre-exposure as a candidate biological mitigation strategy for early DNA damage and oxidative stress endpoints. They do not show that supplementation prevents cancer, cardiovascular disease, or biological aging acceleration.

A randomised, placebo controlled, double-blind antioxidant pre-exposure trial should be nested within the longitudinal biomarker cohort. Candidate regimens (NAC, vitamin C, or a defined antioxidant combination) should be selected through pharmacokinetic and safety review. The intervention should be administered before pre-specified high fluoroscopy sessions or clustered high dose procedural weeks, with endpoints measured before exposure, shortly after, and at defined recovery intervals. Primary endpoints should be acute and subacute biological injury markers (γ-H2AX and 53BP1 foci, micronucleus frequency, oxidative stress markers, inflammatory and SASP cytokines, and cf-mtDNA) rather than biological age clocks alone. Secondary endpoints should include tolerability, adherence, procedural workflow feasibility, and whether repeated biomarker attenuation over time predicts a shallower multi-hallmark aging slope.

 doi:10.20944/preprints202605.0287.v1

ALARA and physical shielding remain the primary risk-reduction hierarchy. A biological mitigation arm must not be presented as permission to accept higher radiation exposure. Governance for Study 5 follows the same principles as Study 4 (Conflicts of Interest section).

Future directions: senolytic therapy. The mechanism described in Section 5 ends in senescent cell accumulation and SASP driven multi-hallmark amplification. Senolytic compounds (notably the dasatinib plus quercetin combination and the natural flavonoid fisetin) selectively eliminate senescent cells in murine models. Both have entered first-in-human trials for senescence associated diseases (Justice et al., 2019; Hickson et al., 2019). A senolytic intervention arm is not proposed here because human safety, dosing, and biomarker response data in non-diseased working populations are not yet adequate to justify enrolling healthy interventional staff. Dasatinib is a chemotherapy agent with substantial toxicities, and the natural flavonoids have not yet shown unequivocal efficacy in healthy adults. Any future senolytic study in interventional staff would require prior evidence of cohort level biological aging signals from Studies 1–4 and independent safety data in healthy adults outside the occupational setting. Rapamycin's extension of lifespan in genetically heterogeneous mice (Harrison et al., 2009) provides therapeutic proof-of-concept that modulating geroconversion has systemic longevity consequences, but it is not proposed here as an occupational intervention.

9. Scope Beyond Interventional Medicine: Inclusion and Exclusion Criteria

Interventional medicine is the founding case. Explicit inclusion and exclusion criteria keep scope bounded as other workforces are added.

Inclusion criteria. A defined occupational exposome that plausibly perturbs multiple interacting hallmarks of aging and is expected to produce measurable changes in pace of biological age, functional reserve, or age-related disease risk. For early cohort selection, plausible perturbation of three or more interacting López-Otín hallmarks is a useful priority threshold. The threshold is provisional and should be refined as evidence accumulates. Single hallmark or single disease exposures fall within occupational medicine but not within this work. A workforce of sufficient size and accessibility is required to support cohort-level biomarker measurement at the scales of Sections 6 and 7. Very small or geographically dispersed workforces may be valid research subjects, but they do not yet support study at the level required by this discipline. Realistic exposure modification or biological augmentation pathways must exist, with the exposure quantifiable and at least partly mitigable.

Exclusion criteria. Acute exposure events (e.g., radiation accidents) are studied within radiation biology and emergency medicine. Single disease occupational research focused on one endpoint (e.g., asbestos-induced mesothelioma, vinyl chloride induced angiosarcoma) remains within classical occupational medicine. General population exposome studies that do not stratify by occupation, and general workforce aging studies that do not condition on a defined occupational exposome, fall within the broader exposome aging literature.

Candidate professions for extension. Several professions appear to satisfy the inclusion criteria. Firefighters inhale a smoke exposome dominated by PAHs and soot, with documented oxidative, inflammatory, and epigenetic effects. IARC reclassified occupational firefighter exposure as Group 1 in 2022, based on sufficient evidence for mesothelioma and bladder cancer and strong mechanistic evidence of genotoxicity, epigenetic alterations, oxidative stress, and chronic inflammation (Demers et al., 2022). Military personnel are exposed to blast trauma, sleep deprivation, chronic psychological stress, and chemical co-exposures. Shift workers experience circadian disruption, a well characterised driver of epigenetic and metabolic aging. Airline crews receive cosmic radiation exposure studied for cancer risk but less systematically for biological aging. Industrial radiographers and nuclear medicine technologists receive occupational radiation doses in the diagnostic range. Sex differences in radiation response have been characterised in murine space radiation models. Female mice are protected from several maladaptive responses (Krukowski et al., 2018), a biological asymmetry relevant to extension cohorts where women are over- or under-represented. All these candidates have

 doi:10.20944/preprints202605.0287.v1

their own partial occupational health literatures. The contribution here is a common hallmarks and biomarkers approach for comparing biological aging across them.

The tiered radiosensitivity approach of Section 8 extends in principle to other high biological hazard professions, but each extension requires profession specific ethical analysis. The physician case is relatively well protected: strong professional society representation, employment stability, established mechanisms for modifying workplace assignments without career termination, and a clinical genetics infrastructure familiar with worker-controlled testing. These conditions are not uniform across firefighting, military service, or other candidate professions, where worker power, union protections, employer discretion, and the history of genetic testing in the occupational context differ substantially. Any extension to these workforces must be developed in partnership with the affected workers and their representative organisations. Worker-controlled results, institutional access limited to aggregate data, and risk adjusted protection (not career restriction) must all be preserved.

10. To the Scientific and Clinical Community

Founding a scientific field requires a community that recognises the question and commits to the research programme. The societies best positioned to carry this work are those with existing competence in the parent disciplines. Occupational medicine bodies (ACOEM, the Faculty of Occupational Medicine, equivalent national bodies) bring epidemiological and clinical infrastructure, and radiation-protection bodies (the Health Physics Society, IRPA, EURADOS) bring dosimetry expertise. Clinical societies in interventional cardiology, electrophysiology, vascular surgery, and interventional radiology (SCAI, HRS, SVS, SIR) represent the founding worker population. The geroscience community has built the hallmarks framework and validated the measurement instruments. The work is feasible only if these communities engage together.

This work also raises an issue that occupational medicine has not formally confronted. Patients undergoing fluoroscopically guided procedures receive documented dose ranges and an informed consent process. The workforce delivering those procedures has not received a comparable document. If biological aging is understood as the progressive loss of physiological resilience and increased vulnerability to chronic disease, occupational exposure should be evaluated as a career long healthspan risk. Workers are not currently told the annual scatter dose they would likely accumulate, the laterality of that exposure, or the evidence base on noncancer morbidity and mortality. Specialty selection happens early in training, often before the trainee has encountered the occupational health literature, and once years of investment have been made the choice becomes difficult to alter.

A translational goal is therefore occupational informed consent grounded in evidence. The document should cover expected lifetime scatter dose, dose laterality, current evidence on noncancer morbidity and mortality, and sex- and ancestry-stratified evidence where it exists. It should also cover individual modifiers of radiation response (including inherited radiosensitivity where the worker has chosen Panel A or Panel B testing) and the limits of current measurement. It should be presented at the point of specialty selection, updated as evidence matures, and owned by the worker. The detailed content, governance, and updating mechanism fall outside this concept paper. As a concrete first step, one of the parent professional bodies (SCAI, ACOEM, IRPA, or a coalition) should convene a working group to scope a feasibility report for the prospective registry of Section 8, Study 1, with informed consent content as a parallel work stream.

11. Conclusions

The empirical aim is narrow and testable: to determine whether and how chronic occupational exposomes accelerate biological aging in defined workforces, and to identify interventions that attenuate that effect. The interventional team is the founding case because the exposome is multi-

 doi:10.20944/preprints202605.0287.v1

agent and at least partially measurable, the mechanism is well characterised in experimental systems, and the workforce is large and accessible enough to support cohort level biomarker work.

The field should be judged by whether its predictions survive prospective testing. Exposed teams should show faster biological aging than matched comparators; the signal should scale with measured dose and, where anatomy permits, with dose laterality; shielding and exposure reduction should attenuate the signal; and risk should extend beyond primary operators to other exposed team members. If these predictions fail, Occupational Geroscience should narrow, change, or disappear. That falsifiability is a strength, not a weakness.

Until these studies are done, neither prevention nor accountability rests on evidence. This research agenda is the empirical contract Occupational Geroscience commits to.

12. Limitations

Three classes of unfinished work qualify the proposal here.

Causal evidence. Biological aging acceleration in interventional staff has not been demonstrated. The mechanistic chain in Section 5 is well characterised at acute high-dose exposures and not yet at chronic occupational low dose rates in working populations. The founding case draws primarily on cardiac catheterisation laboratory staff; generalisation across electrophysiology, neurointerventional radiology, vascular surgery, and interventional oncology will require specialty-specific dosimetric and epidemiological work that this paper does not provide. Operators with high case volume are also self-selected for baseline health and stamina, so any signal observed in an exposed cohort could partly reflect selection rather than exposure. Comparator cohorts of other procedural physicians matched for training intensity, within-cohort analyses of dose response, and pre-specified causal inference methods (propensity-score adjustment; within-person dose laterality contrasts as a quasi-instrument) are required to address this.

Instrument validation. The aging clocks proposed as primary endpoints are population validated cohort level research tools with documented within-individual variability; they are deployed here as cohort level instruments and should not be used for individual diagnosis or occupational decision making. Their sensitivity to detect the modest acceleration plausibly expected at occupational scatter dose levels has not been established. Establishing it is an early empirical task. The same caution applies to cf-mtDNA: its dose–response relationship with chronic low-dose-rate scatter has not been characterised. The proposed multi-omic panel has not been validated as a unified instrument in any occupationally exposed cohort, and most aging estimators were developed in general-population biobanks. SenMayo and other transcriptomic senescence signatures were validated in non-blood tissues. Whether chronic occupational scatter produces the DNA-damage-response selection signature seen in cytotoxic-therapy CHIP is untested.

Governance and equity. The author has a declared commercial interest in radiation-protection products (see Conflicts of Interest). The credibility of any interventional trial depends on independent governance, transparent separation of the conceptual argument from any commercial implication, and treating internal manufacturer dosimetry as hypothesis-generating only. The antioxidant pre-exposure study is a biomarker-validation and biological-mitigation experiment. It is not a recommendation for routine supplementation. Existing data show short-term DNA-damage-marker reductions under specific pre-exposure conditions, but do not establish reduced cancer, cardiovascular, or aging risk. Any protocol requires independent safety review, attention to drug interactions and contraindications, and strict protection against risk compensation.

Sex- and ancestry-stratified analysis is a requirement of this discipline rather than a sensitivity check. It has not been adequately built into the literature for the founding case. Women carry higher radiation-attributable risk for several solid cancers relevant to interventional staff (BEIR VII 2006; ICRP 103 2007). Life Span Study data document sex differences in radiation-related circulatory disease (Shimizu et al., 2010). APOE ε4 confers different dementia risk by ancestral background, with attenuated risk on African relative to European backgrounds (Rajabli et al., 2018). CHIP architecture differs across ancestries, including a TET2 enhancer variant specific to individuals of African ancestry

 doi:10.20944/preprints202605.0287.v1

(Bick et al., 2020). The polygenic radiosensitivity scores behind Panel A were developed predominantly in European-ancestry cohorts and have not been validated for transfer. Cohort designs powered only for the average effect would systematically miss the populations in which the interventions might be most consequential.

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Conflicts of Interest: The author is Founder and CEO of RadProtection Pte. Ltd. (Singapore) and RadProtection Co. Ltd. (Philippines), operating under the brand RadPro, which develops and manufactures radiation-protection products for interventional medicine, including personnel shielding and mobile protection systems. This conflict is declared in full. Readers are encouraged to evaluate the scientific argument independently of this commercial interest. Internal manufacturer dosimetry data from RadPro are hypothesis-generating. They have not been independently replicated or peer-reviewed in the form referenced. Within any trial, these data should be treated as preliminary rather than as primary evidence. Governance principles for the interventional studies (Studies 4 and 5). Both trials must be governed by an independent steering committee free of commercial sponsor representation. Their protocols must be pre-registered and publicly accessible. They must run under ongoing independent safety monitoring. Endpoint adjudication should be blinded where feasible. Results must be publicly reported regardless of outcome. Primary endpoints are biological injury and biomarker measures (DNA-damage foci, micronucleus frequency, oxidative-stress markers, SASP cytokines, cf-mtDNA, and cohort-level pace of biological age), and the trials must be powered accordingly. RadProtection / RadPro and any antioxidant manufacturer must not serve as sponsor, principal investigator, sole funder, statistical analyst, or sole data custodian. Specific antioxidant formulations including Halo may be candidate interventions for testing. Selection should follow independent pharmacokinetic and safety review rather than a sponsor with a commercial interest in the outcome. ALARA and physical shielding remain the primary risk-reduction hierarchy in both trials. Until these studies are completed, both interventions remain research hypotheses rather than clinical or occupational recommendations. Dr. Murphy, an acknowledged contributor to Study 5 design, is the inventor of Halo, an antioxidant formulation named as a candidate intervention. This interest is declared in the Acknowledgements. The author has no financial interest in antioxidant products discussed in Study 5.

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References

Wild CP. Complementing the genome with an 'exposome': the outstanding challenge of environmental exposure measurement in molecular epidemiology. Cancer Epidemiol Biomarkers Prev. 2005;14(8):1847–1850. doi: 10.1158/1055-9965.EPI-05-0456. PMID: 16103423.

 doi:10.20944/preprints202605.0287.v1

López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. The hallmarks of aging. Cell. 2013;153(6):1194–1217. doi: 10.1016/j.cell.2013.05.039. PMID: 23746838.

López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. Hallmarks of aging: an expanding universe. Cell. 2023;186(2):243–278. doi: 10.1016/j.cell.2022.11.001. PMID: 36599349.

Blagosklonny MV. Cell cycle arrest is not yet senescence, which is not just cell cycle arrest: terminology for TOR-driven aging. Aging (Albany NY). 2012;4(3):159–165. doi: 10.18632/aging.100443. PMID: 22394614.

Sampadi B, et al. Divergent molecular and cellular responses to low and high-dose ionizing radiation. Cells. 2022;11(23):3794. doi: 10.3390/cells11233794. PMID: 36497055.

Laberge RM, et al. MTOR regulates the pro-tumorigenic senescence-associated secretory phenotype by promoting IL1A translation. Nat Cell Biol. 2015;17(8):1049–1061. doi: 10.1038/ncb3195. PMID: 26147250.

Andreassi MG, et al. Subclinical carotid atherosclerosis and early vascular aging from long-term low-dose ionizing radiation exposure: a genetic, telomere, and vascular ultrasound study in cardiac catheterization laboratory staff. JACC Cardiovasc Interv. 2015;8(4):616–627. doi: 10.1016/j.jcin.2014.12.233. PMID: 25907089.

Goldstein JA, Balter S, Cowley M, Hodgson J, Klein LW; Interventional Committee of the Society of Cardiovascular Angiography and Interventions. Occupational hazards of interventional cardiologists: prevalence of orthopedic health problems in contemporary practice. Catheter Cardiovasc Interv. 2004;63(4):407–411. doi: 10.1002/ccd.20201. PMID: 15558765.

Klein LW, Tra Y, Garratt KN, Powell W, Lopez-Cruz G, Chambers C, Goldstein JA; Society for Cardiovascular Angiography and Interventions. Occupational health hazards of interventional cardiologists in the current decade: results of the 2014 SCAI membership survey. Catheter Cardiovasc Interv. 2015;86(5):913–924. doi: 10.1002/ccd.25927. PMID: 25810341.

Orme NM, Rihal CS, Gulati R, et al. Occupational health hazards of working in the interventional laboratory: a multisite case control study of physicians and allied staff. J Am Coll Cardiol. 2015;65(8):820–826. doi: 10.1016/j.jacc.2014.11.056. PMID: 25720626.

Monaco MGL, Carta A, Tamhid T, Porru S. Anti-X apron wearing and musculoskeletal problems among healthcare workers: a systematic scoping review. Int J Environ Res Public Health. 2020;17(16):5877. doi: 10.3390/ijerph17165877. PMID: 32823627.

Andreassi MG, Piccaluga E, Guagliumi G, Del Greco M, Gaita F, Picano E. Occupational health risks in cardiac catheterization laboratory workers. Circ Cardiovasc Interv. 2016;9(4):e003273. doi: 10.1161/CIRCINTERVENTIONS.115.003273. PMID: 27072525.

Gillies M, Richardson DB, Cardis E, et al. Mortality from circulatory diseases and other non-cancer outcomes among nuclear workers in France, the United Kingdom and the United States (INWORKS). Radiat Res. 2017;188(3):276–290. doi: 10.1667/RR14608.1. PMID: 28692406.

Roguin A, Goldstein J, Bar O, Goldstein JA. Brain and neck tumors among physicians performing interventional procedures. Am J Cardiol. 2013;111(9):1368–1372. doi: 10.1016/j.amjcard.2012.12.060. PMID: 23419190.

Reeves RR, et al. Invasive cardiologists are exposed to greater left sided cranial radiation: the Brain Radiation Exposure and Attenuation During Invasive Cardiology Procedures (BRAIN) study. JACC Cardiovasc Interv. 2015;8(9):1197–1206. doi: 10.1016/j.jcin.2015.03.027. PMID: 26292583.

Leuraud K, et al. Ionising radiation and risk of death from leukaemia and lymphoma in radiation-monitored workers (INWORKS): an international cohort study. Lancet Haematol. 2015;2(7):e276–281. doi: 10.1016/S2352-3026(15)00094-0. PMID: 26436129.

Finkelstein MM. Is brain cancer an occupational disease of cardiologists? Can J Cardiol. 1998;14(11):1385–1388. PMID: 9854520.

Harrison DE, et al. Rapamycin fed late in life extends lifespan in genetically heterogeneous mice. Nature. 2009;460(7253):392–395. doi: 10.1038/nature08221. PMID: 19587680.

Yu C. Don't be caught half-dressed when working with radiation. Cardiovasc Intervent Radiol. 2020;43(3):369–375. doi: 10.1007/s00270-019-02391-7. PMID: 31844952.

Salavitabar A, Vora AN, Altschul D, et al. ALARA+: Summit on Radiation and Orthopedic Risks in Fluoroscopic Laboratories. Endorsed by ACC, ACVP, ASE, HRS, SCAI, SIR, SNIS, SVIN, and SVS. J Vasc Interv Radiol. 2026;article 108689 (online ahead of print, 24 March 2026). doi: 10.1016/j.jvir.2026.108689. PMID: 41874495.

 doi:10.20944/preprints202605.0287.v1

BEIR VII Phase 2. Health risks from exposure to low levels of ionizing radiation. Washington, DC: National Academies Press; 2006. doi: 10.17226/11340. ISBN-13: 978-0309091565.

ICRP Publication 103. The 2007 recommendations of the International Commission on Radiological Protection. Ann ICRP. 2007;37(2-4):1–332. doi: 10.1016/j.icrp.2007.10.003. PMID: 18082557.

Lu AT, et al. DNA methylation GrimAge strongly predicts lifespan and healthspan. Aging (Albany NY). 2019;11(2):303–327. doi: 10.18632/aging.101684. PMID: 30669119.

Levine ME, et al. An epigenetic biomarker of aging for lifespan and healthspan. Aging (Albany NY). 2018;10(4):573–591. doi: 10.18632/aging.101414. PMID: 29676998.

Belsky DW, et al. DunedinPACE, a DNA methylation biomarker of the pace of aging. eLife. 2022;11:e73420. doi: 10.7554/eLife.73420. PMID: 35029144.

International Commission on Radiological Protection. Individual Radiosensitivity in Radiological Protection. ICRP Task Group 111 Draft Report — Public Consultation Document (not yet a published ICRP recommendation). ICRP; 2025–2026. Available at: https://www.icrp.org [accessed April 2026].

Murphy K, Thakore A, Lacasse MC, Khan DZ. Should future interventional neuroradiologists be screened for mutations that impair radiation-induced DNA repair? Interv Neuroradiol. 2017;23(1):5–7. doi: 10.1177/1591019916662380. PMID: 27815339.

Murphy R, Murphy K. Should interventionalists be screened for genetic mutations that may impair their ability to repair DNA damage from radiation exposure? J Vasc Interv Radiol. 2019;30(11):1830–1831. doi: 10.1016/j.jvir.2019.07.010. PMID: 31655766.

Pandics T, Major D, Fazekas-Pongor V, et al. Exposome and unhealthy aging: environmental drivers from air pollution to occupational exposures. GeroScience. 2023;45(6):3381–3408. doi: 10.1007/s11357-023-00913-3. PMID: 37688657.

Ungvari Z, Tabák AG, Adany R, et al. The Semmelweis Study: a longitudinal occupational cohort study within the framework of the Semmelweis Caring University Model Program for supporting healthy aging. GeroScience. 2024;46(1):191–218. doi: 10.1007/s11357-023-01018-7. PMID: 38060158.

Andrasfay T, Kim JK, Ailshire JA, Crimmins EM. Aging on the job? The association between occupational characteristics and accelerated biological aging. J Gerontol B Psychol Sci Soc Sci. 2023;78(7):1236–1245. doi: 10.1093/geronb/gbad055. PMID: 37004243.

Argentieri MA, Amin N, Nevado-Holgado AJ, et al. Integrating the environmental and genetic architectures of aging and mortality. Nat Med. 2025;31(3):1016–1025. doi: 10.1038/s41591-024-03483-9. PMID: 39972219.

Guogytė K, Plieskienė A, Ladygienė R, et al. Assessment of correlation between chromosomal radiosensitivity of peripheral blood lymphocytes after in vitro irradiation and normal tissue side effects for cancer patients undergoing radiotherapy. Genome Integr. 2017;8:1. doi: 10.4103/2041-9414.198907. PMID: 28250908.

Kerns SL, Kundu S, Oh JH, et al. The prediction of radiotherapy toxicity using single nucleotide polymorphism-based models: a step toward prevention. Semin Radiat Oncol. 2015;25(4):281–291. doi: 10.1016/j.semradonc.2015.05.006. PMID: 26384276.

Andreassen CN, Alsner J. Genetic variants and normal tissue toxicity after radiotherapy: a systematic review. Radiother Oncol. 2009;92(3):299–309. doi: 10.1016/j.radonc.2009.06.015. PMID: 19683821.

Rosenstein BS, West CM, Bentzen SM, et al. Radiogenomics: radiobiology enters the era of big data and team science. Int J Radiat Oncol Biol Phys. 2014;89(4):709–713. doi: 10.1016/j.ijrobp.2014.03.009. PMID: 24969789.

Seibold P, Auvinen A, Averbeck D, et al. Clinical and epidemiological observations on individual radiation sensitivity and susceptibility. Int J Radiat Biol. 2020;96(3):324–339. doi: 10.1080/09553002.2019.1665209. PMID: 31539290.

Higgins-Chen AT, Thrush KL, Wang Y, et al. A computational solution for bolstering reliability of epigenetic clocks: implications for clinical trials and longitudinal tracking. Nat Aging. 2022;2(7):644–661. doi: 10.1038/s43587-022-00248-2. PMID: 36277076.

Kam WW, Banati RB. Effects of ionizing radiation on mitochondria. Free Radic Biol Med. 2013;65:607–619. doi: 10.1016/j.freeradbiomed.2013.07.024. PMID: 23892359.

Kawamura K, Qi F, Kobayashi J. Potential relationship between the biological effects of low-dose irradiation and mitochondrial ROS production. J Radiat Res. 2018;59(Suppl 2):ii91–ii97. doi: 10.1093/jrr/rrx091. PMID: 29415254.

 doi:10.20944/preprints202605.0287.v1

Marazziti D, Tomaiuolo F, Dell'Osso L, et al. Neuropsychological testing in interventional cardiology staff after long-term exposure to ionizing radiation. J Int Neuropsychol Soc. 2015;21(9):670–676. doi: 10.1017/S135561771500082X. PMID: 26400563.

Pantelias A, Terzoudi GI. A standardized G2-assay for the prediction of individual radiosensitivity. Radiother Oncol. 2011;101(1):28–34. doi: 10.1016/j.radonc.2011.09.021. PMID: 22014898.

Picard M, Shirihai OS. Mitochondrial signal transduction. Cell Metab. 2022;34(11):1620–1653. doi: 10.1016/j.cmet.2022.10.008. PMID: 36323233.

Pukkala E, Martinsen JI, Lynge E, et al. Occupation and cancer — follow-up of 15 million people in five Nordic countries. Acta Oncol. 2009;48(5):646–790. doi: 10.1080/02841860902913546. PMID: 19925375.

Demers PA, DeMarini DM, Fent KW, et al. Carcinogenicity of occupational exposure as a firefighter. Lancet Oncol. 2022;23(8):985–986. doi: 10.1016/S1470-2045(22)00390-4. PMID: 35780778.

Carugno M, Maggioni C, Ruggiero V, Crespi E, Monti P, Ferrari L, Pesatori AC. Can night shift work affect biological age? Hints from a cross-sectional study on hospital female nurses. Int J Environ Res Public Health. 2021;18(20):10639. doi: 10.3390/ijerph182010639. PMID: 34682384.

Mwanga HH, Dumas O, Migueres N, Le Moual N, Jeebhay MF. Airway diseases related to the use of cleaning agents in occupational settings. J Allergy Clin Immunol Pract. 2024;12(8):1974–1986. doi: 10.1016/j.jaip.2024.02.036. PMID: 38432401.

Limchantra IV, Fong Y, Melstrom KA. Surgical smoke exposure in operating room personnel: a review. JAMA Surg. 2019;154(10):960–967. doi: 10.1001/jamasurg.2019.2515. PMID: 31433468.

Lee WJ, Jang EJ, Kim KS, Bang YJ. Underestimation of radiation doses by compliance of wearing dosimeters among fluoroscopically-guided interventional medical workers in Korea. Int J Environ Res Public Health. 2022;19(14):8393. doi: 10.3390/ijerph19148393. PMID: 35886244. PMCID: PMC9318991.

Carinou E, Clairand I, Dabin J, Ferrari P, Ginjaume M, Hupe O, Ochoa MG, O'Connor U, Vanhavere F. Individual exposure and monitoring in interventional radiology and cardiology. EURADOS Report 2023-02. Braunschweig: EURADOS; 2023. Available at: https://eurados.sckcen.be/en/news-overview/eurados-report-2023-02-published-individual-exposure-and-monitoring-interventional-radiology-and-cardiology [accessed May 2026].

Trumpff C, Marsland AL, Basualto-Alarcón C, et al. Acute psychological stress increases serum circulating cell-free mitochondrial DNA. Psychoneuroendocrinology. 2019;106:268–276. doi: 10.1016/j.psyneuen.2019.03.026. PMID: 31029929.

United Nations Scientific Committee on the Effects of Atomic Radiation. Sources, Effects and Risks of Ionizing Radiation: UNSCEAR 2020/2021 Report, Annex D — Evaluation of occupational exposure to ionizing radiation. New York: United Nations; 2022. Available at: https://www.unscear.org/unscear/uploads/documents/publications/UNSCEAR_2020_21_Annex-D.pdf [accessed April 2026].

Ibragimova M, Kussainova A, Aripova A, Bersimbaev R, Bulgakova O. The molecular mechanisms in senescent cells induced by natural aging and ionizing radiation. Cells. 2024;13(6):550. doi: 10.3390/cells13060550. PMID: 38534394.

Guan J, Li T, Ma F, Wang N, Zhang H, Li J, Li J, Xu C, Liu Q. DNA damage-dependent mechanisms of ionizing radiation-induced cellular senescence. PeerJ. 2025;13:e20087. doi: 10.7717/peerj.20087. PMID: 41048400.

Li M, You L, Xue J, Lu Y. Ionizing radiation-induced cellular senescence in normal, non-transformed cells and the involved DNA damage response: a mini review. Front Pharmacol. 2018;9:522. doi: 10.3389/fphar.2018.00522. PMID: 29872395.

Sedelnikova OA, Redon CE, Dickey JS, Nakamura AJ, Georgakilas AG, Bonner WM. Role of oxidatively induced DNA lesions in human pathogenesis. Mutat Res. 2010;704(1-3):152–159. doi: 10.1016/j.mrrev.2009.12.005. PMID: 20060490.

Georgakilas AG, O'Neill P, Stewart RD. Induction and repair of clustered DNA lesions: what do we know so far? Radiat Res. 2013;180(1):100–109. doi: 10.1667/RR3041.1. PMID: 23682596.

Sutherland BM, Bennett PV, Sidorkina O, Laval J. Clustered DNA damages induced in isolated DNA and in human cells by low doses of ionizing radiation. Proc Natl Acad Sci U S A. 2000;97(1):103–108. doi: 10.1073/pnas.97.1.103. PMID: 10618378.

 doi:10.20944/preprints202605.0287.v1

Eccles LJ, O'Neill P, Lomax ME. Delayed repair of radiation induced clustered DNA damage: friend or foe? Mutat Res. 2011;711(1-2):134–141. doi: 10.1016/j.mrfmmm.2010.11.003. PMID: 21130102.

Dvorkin S, Cambier S, Volkman HE, Stetson DB. New frontiers in the cGAS-STING intracellular DNA-sensing pathway. Immunity. 2024;57(4):718–730. doi: 10.1016/j.immuni.2024.02.019. PMID: 38599167.

Barnes PJ. Cellular senescence as a mechanism and target in chronic lung diseases. Am J Respir Crit Care Med. 2019;200(5):556–564. doi: 10.1164/rccm.201810-1975TR. PMID: 30860857.

Zhavoronkov A, Ying K, Wilczok D. Peakspan: defining, quantifying and extending the boundaries of peak productive lifespan. Aging Dis. 2026 Feb 25. doi: 10.14336/AD.2026.0080. PMID: 41747171. Online ahead of print.

Kuefner MA, Brand M, Ehrlich J, Braga L, Uder M, Semelka RC. Effect of antioxidants on x-ray-induced γ-H2AX foci in human blood lymphocytes: preliminary observations. Radiology. 2012;264(1):59–67. doi: 10.1148/radiol.12111730. PMID: 22509049.

Brand M, Sommer M, Ellmann S, Wuest W, May MS, Eller A, Vogt S, Lell MM, Kuefner MA, Uder M. Influence of different antioxidants on X-ray induced DNA double-strand breaks (DSBs) using γ-H2AX immunofluorescence microscopy in a preliminary study. PLoS One. 2015;10(5):e0127142. doi: 10.1371/journal.pone.0127142. PMID: 25996998.

Velauthapillai N, Barfett J, Jaffer H, Mikulis D, Murphy K. Antioxidants taken orally prior to diagnostic radiation exposure can prevent DNA injury. J Vasc Interv Radiol. 2017;28(3):406–411. doi: 10.1016/j.jvir.2016.10.022. PMID: 28034704.

Andreassi MG, Cioppa A, Manfredi S, Neri MG, Foffa I, Picano E. N-acetyl cysteine reduces chromosomal DNA damage in circulating lymphocytes during cardiac catheterization procedures: a pilot study. Int J Cardiol. 2012;161(2):93–96. doi: 10.1016/j.ijcard.2011.05.001. PMID: 21605919.

Oh HS, Rutledge J, Nachun D, et al. Organ aging signatures in the plasma proteome track health and disease. Nature. 2023;624(7990):164–172. doi: 10.1038/s41586-023-06802-1. PMID: 38057571.

Kivimäki M, Frank P, Pentti J, et al. Proteomic organ-specific ageing signatures and 20-year risk of age-related diseases: the Whitehall II observational cohort study. Lancet Digit Health. 2025;7(3):e195–e204. doi: 10.1016/j.landig.2025.01.006. PMID: 40015764.

Lehallier B, Gate D, Schaum N, et al. Undulating changes in human plasma proteome profiles across the lifespan. Nat Med. 2019;25(12):1843–1850. doi: 10.1038/s41591-019-0673-2. PMID: 31806903.

Sayed N, Huang Y, Nguyen K, et al. An inflammatory aging clock (iAge) based on deep learning tracks multimorbidity, immunosenescence, frailty and cardiovascular aging. Nat Aging. 2021;1(7):598–615. doi: 10.1038/s43587-021-00082-y. PMID: 34888528.

van den Akker EB, Trompet S, Barkey Wolf JJH, et al. Metabolic age based on the BBMRI-NL ^{1}H-NMR metabolomics repository as biomarker of age-related disease. Circ Genom Precis Med. 2020;13(5):541–547. doi: 10.1161/CIRCGEN.119.002610. PMID: 33079603.

Deelen J, Kettunen J, Fischer K, et al. A metabolic profile of all-cause mortality risk identified in an observational study of 44,168 individuals. Nat Commun. 2019;10(1):3346. doi: 10.1038/s41467-019-11311-9. PMID: 31431621.

Krištić J, Vučković F, Menni C, et al. Glycans are a novel biomarker of chronological and biological ages. J Gerontol A Biol Sci Med Sci. 2014;69(7):779–789. doi: 10.1093/gerona/glt190. PMID: 24325898.

Saul D, Kosinsky RL, Atkinson EJ, et al. A new gene set identifies senescent cells and predicts senescence-associated pathways across tissues. Nat Commun. 2022;13(1):4827. doi: 10.1038/s41467-022-32552-1. PMID: 35974106.

Jaiswal S, Fontanillas P, Flannick J, et al. Age-related clonal hematopoiesis associated with adverse outcomes. N Engl J Med. 2014;371(26):2488–2498. doi: 10.1056/NEJMoa1408617. PMID: 25426837.

Genovese G, Kähler AK, Handsaker RE, et al. Clonal hematopoiesis and blood-cancer risk inferred from blood DNA sequence. N Engl J Med. 2014;371(26):2477–2487. doi: 10.1056/NEJMoa1409405. PMID: 25426838.

Hsu JI, Dayaram T, Tovy A, et al. PPM1D mutations drive clonal hematopoiesis in response to cytotoxic chemotherapy. Cell Stem Cell. 2018;23(5):700–713.e6. doi: 10.1016/j.stem.2018.10.004. PMID: 30388424.

Bolton KL, Ptashkin RN, Gao T, et al. Cancer therapy shapes the fitness landscape of clonal hematopoiesis. Nat Genet. 2020;52(11):1219–1226. doi: 10.1038/s41588-020-00710-0. PMID: 33106634.

 doi:10.20944/preprints202605.0287.v1

Justice JN, Nambiar AM, Tchkonia T, et al. Senolytics in idiopathic pulmonary fibrosis: results from a first-in-human, open-label, pilot study. EBioMedicine. 2019;40:554–563. doi: 10.1016/j.ebiom.2018.12.052. PMID: 30616998.

Hickson LJ, Langhi Prata LGP, Bobart SA, et al. Senolytics decrease senescent cells in humans: preliminary report from a clinical trial of dasatinib plus quercetin in individuals with diabetic kidney disease. EBioMedicine. 2019;47:446–456. doi: 10.1016/j.ebiom.2019.08.069. PMID: 31542391.

Shimizu Y, Kodama K, Nishi N, et al. Radiation exposure and circulatory disease risk: Hiroshima and Nagasaki atomic bomb survivor data, 1950–2003. BMJ. 2010;340:b5349. doi: 10.1136/bmj.b5349. PMID: 20075151.

Krukowski K, Grue K, Frias ES, et al. Female mice are protected from space radiation-induced maladaptive responses. Brain Behav Immun. 2018;74:106–120. doi: 10.1016/j.bbi.2018.08.008. PMID: 30107198.

Rajabli F, Feliciano BE, Celis K, et al. Ancestral origin of ApoE ε4 Alzheimer disease risk in Puerto Rican and African American populations. PLoS Genet. 2018;14(12):e1007791. doi: 10.1371/journal.pgen.1007791. PMID: 30517106.

Bick AG, Weinstock JS, Nandakumar SK, et al. Inherited causes of clonal haematopoiesis in 97,691 whole genomes. Nature. 2020;586(7831):763–768. doi: 10.1038/s41586-020-2819-2. PMID: 33057201.