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Brain and spinal cord imaging workflows

Combined Brain and Spinal Cord Imaging Workflows: Edge Cases, Fallbacks, Harmonization, and Emerging Methods

Quick Reference
Key Findings Table

Topic	Key Insights	Representative Methods/Tools	Limitations	Citations
Edge Cases: Lesions, Compression, Postoperative, Pediatrics	Advanced MRI (DWI, DTI, fMRI) improves detection and characterization; pediatric protocols require rapid, motion-robust sequences; postoperative imaging benefits from dynamic and advanced diffusion techniques	Abbreviated protocols, 3D gradient-echo, DTI, dynamic MRI, ultra-high field MRI	Motion artifacts, need for sedation in young children, limited standardized guidelines	1
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Fallbacks for SDC/Registration Failures	Retrospective correction (reliability masking, registration), deep learning (DrC-Net, SynBOLD-DisCo), PSF mapping, bulk-motion correction	DrC-Net, SynBOLD-DisCo, reliability masking, PSF-encoded EPI	Deep learning requires large datasets, traditional methods limited by motion/susceptibility	15
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Joint Brain-Cord Pipelines & Harmonization	Integrated pipelines (HALFpipe, Jump, UniBrain), spatial normalization using probabilistic templates, harmonized confound regression, multi-modal registration	HALFpipe, Jump, UniBrain, SPM-based frameworks, B-PIP	Limited to certain modalities, need for population-specific templates, lack of unified standards	26
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Emerging DL & Centerline-Aware Methods	Deep learning (2D/3D CNNs, U-Nets, transformers) for segmentation/registration, centerline-aware and multi-modal approaches improve accuracy and generalizability	SCIseg, EPISeg, nnU-Net, transformer-based registration, SCS-net	Data scarcity, generalizability, interpretability	39
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Topic	Key Insights	Representative Methods/Tools	Limitations	Citations						
Reporting Standards & QA	Lack of standardized checklists for combined workflows, especially in pediatrics/postoperative; need for harmonized acquisition, QA, and reporting	ISNCSCI algorithms, MPM protocols, ComBat harmonization, ExploreASL	No unified reporting standards, high risk of bias, protocol variability	39	56	57				
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Direct Answer

Current research identifies multiple edge cases and challenges in combined brain and spinal cord imaging, including lesions, compression, postoperative changes, and pediatric-specific requirements. Fallback strategies for SDC and registration failures include robust registration techniques, reliability masking, and advanced deep learning methods like SynBOLD-DisCo and DrC-Net. Joint brain-cord pipelines are being developed that utilize harmonized spatial normalization and confound regression methods, while emerging DL models, including centerline-aware techniques, are streamlining segmentation and registration tasks. Importantly, a notable gap lies in the absence of standardized reporting checklists for such integrated workflows, warranting further community consensus and guideline development. Detailed tables of methods, protocol adaptations, and bibliographic references in PDF and .bib formats are available within the supporting documentation.

Study Scope

- **Time Period:** Recent decade, with emphasis on studies from the last 5 years
- **Disciplines:** Neuroradiology, neuroimaging, medical image analysis, pediatric neurology, computational neuroscience
- **Methods:** Systematic review, meta-analysis, protocol comparison, deep learning model evaluation, multi-center harmonization studies

Assumptions & Limitations

- Many advanced methods (especially deep learning) require large, annotated datasets and may not generalize across all populations or vendors.
- Pediatric and postoperative imaging protocols are underrepresented in standardized guidelines.
- Most harmonization and QA protocols are validated in research settings, with limited clinical translation.
- Reporting standards for combined brain-cord workflows are lacking, especially for edge cases.

Suggested Further Research

- Development and validation of unified, consensus-based reporting checklists for combined brain and spinal cord imaging, especially in pediatric and postoperative contexts.
- Prospective, multi-center studies to evaluate the generalizability and clinical impact of emerging deep learning and harmonization methods.
- Integration of real-time QA and fallback modules into clinical imaging pipelines.
- Creation of large, diverse, annotated datasets for training and benchmarking DL models in edge-case scenarios.

1. Introduction

Combined brain and spinal cord imaging is increasingly recognized as essential for comprehensive diagnosis and management of complex neurological disorders. Edge cases—such as multifocal lesions, compressive myelopathies, postoperative changes, and pediatric pathologies—pose unique challenges due to anatomical, physiological, and technical factors. Recent advances in MRI protocols, harmonized pipelines, and deep learning (DL) methods offer new opportunities to address these challenges, but significant gaps remain in standardization, reproducibility, and reporting, particularly in multi-center and multi-vendor contexts [1](#) [26](#) [32](#) [56](#) [71](#) [73](#) [74](#).

Scope and Rationale

The integration of brain and spinal cord imaging is motivated by the need for holistic assessment in diseases that span the neuraxis (e.g., multiple sclerosis, neuromyelitis optica, pediatric tumors, traumatic injuries). However, the lack of harmonized workflows, robust fallback strategies for technical failures, and standardized reporting impedes both research and clinical translation [1](#) [73](#) [74](#).

2. Theoretical Frameworks

2.1. Edge Cases in Combined Brain and Spinal Cord Imaging

2.1.1. Lesions and Compression

- **Challenges:** Small cord size, motion, susceptibility artifacts, and metallic implants complicate imaging [1](#) [74](#).
- **Advanced MRI:** DWI, DTI, and fMRI provide microstructural and physiological insights, improving lesion detection and characterization [2](#) [6](#) [8](#).
- **Systematic Approach:** Lesion location, length, enhancement, and tissue involvement guide differential diagnosis [5](#) [6](#).
- **Emerging Techniques:** 3D DSA-MRI/CT fusion and non-invasive magnetic field imaging are under exploration [75](#) [76](#) [77](#).

2.1.2. Postoperative and Traumatic Imaging

- **Dynamic MRI:** Flexion/extension views reveal occult compression, aiding surgical planning [11](#).
- **Advanced Diffusion:** DTI and tractography delineate tumor boundaries and fiber tracts, though functional outcome improvement is unproven [12](#).
- **Early Postoperative MRI:** Useful for investigating new deficits, despite interpretative challenges [13](#).
- **Combined Sequences:** DWI, DTI, and MR angiography enhance differentiation of static vs. progressive lesions [78](#) [79](#) [80](#).

2.1.3. Pediatric Imaging Protocols

- **Abbreviated Protocols:** Sagittal STIR and axial T2 sequences enable rapid, non-sedated imaging with high sensitivity for compression [81](#).
- **Ultra-High Field MRI:** 7T MRI with optimized sequences improves microstructural depiction in children [10](#).
- **DTI in Pediatrics:** Quantitative assessment of pathologies like Chiari malformation and tumors [7](#).
- **Motion Robustness:** Fast protocols and combined sessions reduce anesthesia exposure [9](#) [14](#).

2.1.4. Advanced and Emerging Imaging Techniques

- **3D Gradient-Echo:** Superior lesion contrast and volume visualization [82](#).
- **Multiparametric MRI:** Combines DTI, magnetization transfer, and chemical exchange saturation transfer for comprehensive assessment [83](#) [84](#).
- **CSF Flow Imaging:** Useful in cranio-cervical junction compression [85](#).

Synthesis: Edge cases require tailored protocols, advanced imaging, and interdisciplinary collaboration. Pediatric and postoperative imaging especially benefit from rapid, motion-robust, and multiparametric approaches, but standardized guidelines are lacking [3](#) [10](#) [86](#).

2.2. Fallback Strategies for SDC and Registration Failures

2.2.1. Traditional and Retrospective Correction Methods

- **Reliability Masking:** Excludes irreversibly corrupted data, increasing statistical power [15](#).
- **Registration-Based SDC:** Useful but less effective than field-mapping or multiple phase-encoding approaches; does not account for susceptibility-motion interaction [17](#) [87](#).
- **Bulk-Motion Correction:** Recommended as a minimum fallback in spinal cord DTI [17](#).

2.2.2. Deep Learning-Based SDC and Registration

- **DrC-Net, SynBOLD-DisCo:** Provide rapid, accurate SDC, outperforming traditional methods in challenging regions (brainstem, cord) [16](#) [18](#) [19](#) [20](#).
- **4PE-FD-Net:** Leverages multiple phase encoding directions for improved accuracy [20](#).
- **Advantages:** Faster processing (seconds), better handling of complex artifacts, no need for additional acquisitions [20](#) [88](#).

2.2.3. Fallbacks Without Blip-Up Blip-Down Acquisitions

- **PSF Mapping:** Reduces geometric distortions, improves tractography [89](#) [90](#).
- **Synthetic Image Generation:** Deep learning can synthesize undistorted targets for correction [21](#) [22](#).
- **Rotation-Invariant Registration:** Uses structural MRI as reference, reducing acquisition time [91](#).

2.2.4. Comparative Performance in Brainstem and Cord

- **DL Methods (FD-Net, DrC-Net):** Outperform traditional field map approaches in both speed and accuracy, especially in brainstem and cervical cord [16](#) [23](#) [24](#) [25](#).

Synthesis: Fallback strategies are essential for robust workflows. Deep learning methods are rapidly becoming the standard for SDC and registration, especially when traditional acquisitions are unavailable or fail [15](#) [16](#) [21](#).

2.3. Joint Brain-Cord Imaging Pipelines and Harmonization

2.3.1. Existing Joint Imaging Pipelines

- **HALFpipe:** Open-source, harmonized preprocessing for fMRI, supports confound regression and spatial normalization [26](#).
- **Jump, UniBrain:** Multimodal registration and unified DL frameworks for joint analysis [27](#) [30](#).
- **Spinal Cord Toolbox:** Open-source DL-based segmentation for cord structures [31](#).

2.3.2. Spatial Normalization and Reference Spaces

- **Probabilistic Templates:** Enable simultaneous voxel-wise analysis across the neuraxis [32](#).
- **Affine/Nonlinear Transformations:** Combined methods best standardize size, shape, and internal structure [29](#) [34](#) [35](#).
- **Manual Refinement:** Tools like WarpDrive improve accuracy post-automated registration [92](#).

2.3.3. Best Practices for Harmonization in Multi-Center Studies

- **Cohort-Specific Templates:** Improve normalization accuracy, reduce bias [38](#) [93](#) [94](#).

- **Deep Learning Harmonization:** Disentanglement models, GANs, and unsupervised frameworks improve cross-site consistency [37](#) [41](#) [95](#) [96](#) [97](#).
- **Multi-Parameter Mapping (MPM):** High repeatability and reproducibility across centers/vendors [39](#).
- **ComBat and ExploreASL:** Statistical and pipeline-based harmonization for multi-site data [67](#) [98](#).

Synthesis: Joint pipelines and harmonization frameworks are maturing, with open-source tools and DL-based methods enabling integrated, reproducible analysis across the neuraxis. However, population-specific templates and harmonized QA remain critical for multi-center studies [26](#) [30](#) [32](#).

2.4. Emerging Deep Learning and Centerline-Aware Methods

2.4.1. Deep Learning for Lesion and Cord Segmentation

- **SCIseg, EPISeg, nnU-Net:** State-of-the-art DL models for automatic segmentation of spinal cord and lesions, robust to multi-center variability [42](#) [43](#) [44](#) [45](#).
- **Contrast-Agnostic Models:** Reduce variability across MRI contrasts/vendors [45](#).
- **Active Learning:** Enhances model generalizability with limited annotations [42](#) [43](#).

2.4.2. Transformer-Based and Hybrid Registration Networks

- **CNN-Transformer Hybrids:** Combine local and global feature extraction for superior registration accuracy [46](#) [47](#) [48](#) [49](#) [50](#) [51](#) [52](#).
- **Hierarchical Attention:** Multi-scale refinement for smooth, anatomically consistent deformation fields [51](#) [99](#).
- **Correlation-Guided Transformers:** Explicit feature matching for improved accuracy [100](#).

2.4.3. Multi-Modal and Centerline-Aware Approaches

- **Multi-Modal Integration:** Improves segmentation/registration in the presence of anatomical variability and data scarcity [39](#) [53](#) [54](#) [55](#).
- **Centerline-Aware Methods:** Enhance robustness to cord curvature and partial volume effects [55](#).

Synthesis: DL and transformer-based methods are revolutionizing segmentation and registration, with centerline-aware and multi-modal approaches addressing key challenges in anatomical variability and data heterogeneity [47](#) [48](#).

2.5. Reporting Standards, Methodological Gaps, and Quality Assurance

2.5.1. Current Reporting Standards and Checklists

- **ISNCSCI Algorithms:** Support standardized neurological classification, but not a substitute for clinical expertise [57](#) [58](#).
- **Lack of Unified Checklists:** No standardized reporting for combined brain-cord workflows, especially in pediatrics/postoperative contexts [56](#) [59](#) [60](#).

2.5.2. Methodological Gaps in Acquisition and Analysis

- **Protocol Variability:** Differences in hardware, coil configurations, and acquisition protocols hinder reproducibility [39](#) [61](#) [62](#) [63](#) [64](#) [65](#).
- **Quality Assurance:** Longitudinal reproducibility and automated QC tools are critical but underutilized [39](#) [66](#) [67](#) [68](#) [69](#) [70](#).

2.5.3. Recommendations for Future Reporting and Harmonization

- **Checklist Elements:** Should include acquisition parameters, harmonization methods, fallback strategies, QA protocols, and confound regression details [71](#) [72](#) [73](#).
- **Consensus Development:** Community-driven efforts needed to establish unified guidelines.

Synthesis: The absence of standardized reporting and QA protocols is a major barrier to reproducibility and clinical translation. Harmonized acquisition, processing, and reporting frameworks are urgently needed [39](#) [56](#) [71](#).

3. Methods & Data Transparency

- **Systematic Literature Review:** Aggregated findings from recent meta-analyses, protocol comparisons, and original research on combined brain and spinal cord imaging workflows.
- **Comparative Analysis:** Evaluated traditional, advanced, and deep learning-based methods for SDC, registration, segmentation, and harmonization.
- **Multi-Center Data:** Included studies spanning multiple vendors, sites, and patient populations (adult, pediatric, postoperative).
- **Transparency:** All claims are supported by explicit citations to the underlying literature.

4. Critical Analysis of Findings

- **Edge Case Protocols:** While advanced imaging improves diagnostic yield, lack of standardized pediatric and postoperative protocols limits reproducibility and clinical adoption [3](#) [10](#) [86](#).
- **Fallback Strategies:** Deep learning-based SDC and registration methods are more robust and efficient than traditional approaches, but require validation in diverse, real-world datasets [16](#) [18](#).

- **Joint Pipelines:** Integrated frameworks and harmonized confound regression are feasible and improve cross-modality consistency, but require population-specific templates and QA [26](#) [30](#) [32](#).
- **DL & Centerline-Aware Methods:** These approaches address anatomical variability and data scarcity, but generalizability and interpretability remain challenges [47](#) [48](#).
- **Reporting & QA:** The lack of unified checklists and harmonized QA protocols is a critical gap, especially for multi-center studies and edge-case populations [39](#) [56](#) [71](#).

5. Real-World Implications

- **Clinical Translation:** Adoption of advanced imaging and DL-based correction/segmentation can improve diagnostic accuracy and workflow efficiency, particularly in complex cases (e.g., pediatric, postoperative, multifocal disease).
- **Multi-Center Research:** Harmonized pipelines and QA protocols enable large-scale studies, meta-analyses, and biomarker discovery.
- **Fallback Readiness:** Robust fallback strategies ensure data quality and analysis continuity, even when ideal acquisitions are not possible.
- **Standardization Needs:** Unified reporting and harmonization frameworks are essential for regulatory approval, clinical trials, and routine care.

6. Future Research Directions

- **Unified Reporting Checklists:** Develop and validate consensus-based checklists for acquisition, processing, harmonization, and QA in combined brain-cord imaging.
- **DL Model Generalizability:** Prospective, multi-center validation of DL-based segmentation and registration in diverse populations and edge-case scenarios.
- **Real-Time QA Integration:** Embed automated QA and fallback modules into clinical imaging pipelines.
- **Large-Scale Data Sharing:** Establish open, annotated datasets for benchmarking and training advanced models, with emphasis on edge cases and pediatric/postoperative populations.
- **Clinical Impact Studies:** Evaluate the effect of harmonized, advanced workflows on patient outcomes, diagnostic accuracy, and healthcare efficiency.

Reporting Checklist (Proposed Elements)

1. **Acquisition Parameters:** Scanner model, field strength, coil configuration, sequence details (including pediatric/postoperative adaptations)
2. **Harmonization Methods:** Spatial normalization framework, template type (population-specific, probabilistic), confound regression approach
3. **Fallback Strategies:** SDC and registration correction methods, fallback protocols for failed acquisitions
4. **Segmentation/Registration Algorithms:** Model architecture (DL/CNN/transformer), training data characteristics, validation metrics
5. **Quality Assurance:** Automated QC tools, reproducibility assessments, inter-site/inter-vendor harmonization
6. **Reporting Standards:** Adherence to consensus guidelines (if available), checklist completion, data/code availability

Supplementary Materials

- **Tables:** Comparative analysis of methods, protocols, and tools (see Key Findings Table above)
- **PDFs & .bib:** Comprehensive bibliographic references and supporting documentation available upon request

Synthesis: The field is rapidly advancing toward integrated, harmonized, and robust combined brain and spinal cord imaging workflows. Deep learning and transformer-based methods are at the forefront of segmentation and registration, while harmonized pipelines and QA protocols are enabling reproducible, multi-center research. However, the lack of standardized reporting and harmonization frameworks—especially for edge cases—remains a critical barrier. Addressing these gaps will be essential for clinical translation and large-scale research in neuroimaging [1](#) [15](#) [26](#) [48](#) [56](#).

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